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PREFACE

The work described in this report was authorized under Project 1M162622A554, Chemical Munitions and Chemical Combat Support; Technical Area 4-5, Smoke Toxicology. The work was started in July 1978 and completed in May 1980. The experimental data are contained in notebook 9839.

In conducting the research described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals" as promulgated by the Committee on Revision of the Guide for Laboratory Animals Facilities and Care of the Institute of Laboratory Animal Resources, National Research Council.

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THE SUBCHRONIC EFFECTS OF REPEATED EXPOSURE TO WHITE PHOSPHORUS/FELT SCREENING SMOKES IN RATS

1. INTRODUCTION

Toxicity studies were conducted to determine the subchronic effects of repeated exposure to three concentration levels of a white phosphorus screening smoke. This smoke, one of the candidate screening smokes, was generated by burning pieces of white phosphorus-impregnated felt.

The following studies were performed to obtain a subchronic toxicity profile on rats: inhalation toxicity of multiple exposures, including pathology, hematology, and blood chemistry, and effects of exposures on reproduction, behavior, and physiology.

2. EXPERIMENTAL PROCEDURES

2.1 Chamber operation and sample collection.

Animals for the inhalation studies were placed in compartmented stainless-steel wire-mesh cages. The cages were put on racks in a 20-cubic-meter exposure chamber.

Military grade white phosphorus, which had been forced under pressure into thick pieces of wool felt, was cut into cubes having specific weights. For each exposure, one of these cubes on an aluminum foil pan of a known weight was placed on an electric hotplate within the chamber. The hotplate was a fast-heating unit capable of temperatures in excess of 700°F.

The chamber door was closed and sealed, and the chamber exhaust system was shut down. The hotplate was plugged in and the white phosphorus/felt ignited, usually in less than 2 minutes, producing a dense white smoke. This smoke is made up of a number of oxides of phosphorus: $P_4O \cdot P_2O \cdot P_2O_3$ (or P_4O_6), PO_2 (or P_2O_4), P_2O_5 (or P_4O_{10}), and P_2O_6 ; but only three of these species - P_2O_3 , PO_2 , and P_2O_5 - are well established.¹ All three of these oxides are deliquescent and they could, therefore, contribute various aqueous droplets to the smoke. The reaction of P_2O_5 with atmospheric moisture has already been described; the corresponding reaction for P_2O_3 produces o-phosphorus acid. The tetraoxide, P_2O_4 , reacts with water to produce equimolar solutions of o-phosphorous and o-phosphoric acid.¹ The white phosphorus/felt burning time ranged from less than 1 minute for some of the small cubes to over 9 minutes for one of the large cubes. The smoke was contained within the chamber for 15 minutes before being removed by the exhaust system.

Smoke sampling started after 7 minutes of exposure. The samples were collected on Gelman Type-A glass fiber filter pads. Twelve liters of chamber air, at the rate of 3 liters per minute, were drawn through the filter pads contained in the air sampler probe. The filter pads were placed in Erlenmeyer flasks. Particulate material was extracted with distilled water, boiled for 10 minutes, and titrated for phosphoric acid content (see appendix A).

Air samples were also collected in a modified Rochester cascade impactor and analyzed for phosphoric acid content, and the mass median diameter of the airborne particles was derived.

2.2 Animals used.

Four groups of Sprague-Dawley rats were used, one for each dose level plus the controls. Thirty-six male and 36 female rats were used for the high- and intermediate-exposure levels with 18 rats of each sex acting as controls for each level. Only 18 males and a like number of females were exposed to the low-dose level. Nine animals of each sex acted as controls for this exposure.

Additional groups of rats were exposed and the rats were mated on different schedules to determine the effects of repeated exposures on mammalian germ cells and reproductive performance. Procedures used are discussed in a previous report.*

2.3 Animal exposures and observations.

Animals were exposed for 15 minutes daily, 5 days a week for 13 weeks. The rats were observed for toxic signs before and after each exposure. At regular intervals during the 13-week exposure and 4-week postexposure periods, all animals were weighed.

After 6 weeks, one-third of the animals were withdrawn from exposure. Half of these animals were bled and submitted to pathology. The other half were examined to see if any physiological or behavioral changes occurred. When the 13 weeks of exposure ended, the remaining animals were separated into two groups. One group was divided as were the 6-week animals with half going to pathology and half for physiological and behavioral studies. The remaining animals were held for a 4-week postexposure period to observe any recovery that might occur. Then they were bled and submitted for pathological evaluation.

2.4 Blood studies.

Blood samples in rats were analyzed for triglycerides, cholesterol, glucose, urea nitrogen, creatinine, uric acid, sodium, potassium, chloride, carbon dioxide, alkaline phosphatase, albumin, globulin, calcium, phosphorus, serum glutamic pyruvic transaminase, serum glutamic oxalacetic transaminase, red blood cell count, white blood cell count, differential white blood cell count, hematocrit, and hemoglobin.

2.5 Pathology.

Gross and microscopic pathological examinations of the following body organs were performed for all animals submitted: heart, lung, liver, spleen, kidney, brain, eye, trachea, nasal turbinate, adrenal, stomach, urinary bladder, pancreas, thyroid, esophagus, duodenum, colon, lymph node, thymus, testis, epididymus, ovary, uterus, bone marrow, and skin. In addition to those animals sacrificed at 6, 13, and 17 weeks, animals that died during the experiments were submitted for necropsies. The number sacrificed at each time interval was adjusted according to the number of animals that died during that interval.

*Starke, W. C., and Pellerin, R. J. Technical Memorandum. The Effects of CS-2 on Reproduction in Rats (in preparation). 1980.

2.6 Physiological and behavioral studies.

Animals were submitted for physiological and behavioral evaluations using the procedures described in a previous publication.²

3. RESULTS

3.1 Exposure conditions.

Target concentrations were 1000, 500, and 200 mg/m³. Target and actual concentrations are used interchangeably in the appendixes. Concentrations are also referred to as high, intermediate, and low, respectively. To obtain desired concentrations, 20-, 10-, or 3-gram cubes of the white phosphorus-impregnated felt were used. When ignited, a dense white smoke-like mist was produced. The droplets of this mist had a mass median diameter of 0.5 micron. A charred residue weighing approximately 27% of the original weight remained after burning.

Appendix B, table B-1, shows the mean exposure doses produced by each cube recorded.

3.2 Toxic signs.

Animals were not visible for observation until the smoke cloud was evacuated from the chamber. Visible toxic signs were not observed during the first 3 days of exposure to the high dose. One hour after the fourth exposure one female rat died. Two other rats wheezed for about 2 hours. Of the 72 rats starting this high-dose study, 23 died during the first 6 weeks of exposure. Four more died during the remaining 7 weeks. Transitory dyspnea and wheezing were observed in many rats, with recovery within 2 hours of each exposure. The cumulative exposures at which deaths occurred are shown in appendix B, table B-2.

Rats exposed to the intermediate and low doses showed no visible toxic signs. None of these animals died.

3.3 Body-organ weights.

There were no consistent changes in total body weights or in weights of the organs regardless of dose or time. Means and standard errors for body and organ weights of control and exposed rats are shown in tables B-3 and B-4, appendix B. Significant differences, where they did occur, are indicated.

3.4 Hematology and blood chemistry.

No agent-related changes were observed in the blood chemistry and hematology analyses. "T" test evaluations indicated there were no significant agent-related differences between control and exposed values. No sex-related changes were observed. Means and standard errors of all blood constituents analyzed are shown in tables B-5 through B-10, appendix B.

3.5 Pathology.

3.5.1 Spontaneous deaths.

A high mortality rate (about 40%) occurred in the group of colony rats exposed to the 1161 mg/m³ dose level. The deaths appear to be agent and dose related. None of the rats exposed to the intermediate- or low-dose levels died. A complete description of pathological findings is presented in appendix C.

3.5.2 Six-week exposure.

Although laryngitis or tracheitis was not observed in any of the control animals, all laryngeal and tracheal specimens from rats exposed to the high-dose level displayed a moderate-to-severe laryngitis/tracheitis. Fifty percent of the rats receiving the intermediate-dose level displayed a minimal-to-mild tracheitis while one-third had a mild laryngitis. Only one rat receiving the low dose displayed tracheitis. Four of six high-dose rats had a minimal-to-severe interstitial pneumonia. Two of the 18 control rats displayed a minimal interstitial pneumonia. A complete description of these pathological findings is presented in appendix D.

3.5.3 Thirteen-week exposure.

Although none of the control rats displayed laryngitis or tracheitis, all of the male rats receiving the high-dosage level of white phosphorus/felt exhibited a moderate laryngitis. Of the female rats receiving the same dosage level (1161 mg/m³) of white phosphorus/felt, one of two larynges examined displayed a moderate laryngitis; whereas two out of three tracheae displayed mild-to-moderate tracheitis. Three out of six female rats receiving the medium-dosage level of white phosphorus/felt displayed a moderate tracheitis; whereas three out of five male rats receiving the same level exposure displayed slight-to-moderate tracheitis. None of the low-dosage-level animals displayed laryngitis or tracheitis. A complete description of these pathological findings is presented in appendix E.

3.5.4 Thirteen-week exposure with four-week recovery period.

Significant findings were limited to the respiratory tracts of the rats exposed to the high- and intermediate-dose levels. Lesions were noted in the larynx or trachea of 15 of 16 high-dose rats and 20 of 24 intermediate-dose rats. Pulmonary lesions were noted in 11 of 16 high-dose and 6 of 24 intermediate-dose rats. None of the control or low-dose animals exhibited significant lesions. A complete description of these pathological findings is presented in appendix F.

3.6 Reproduction studies.

To assess the effects of white phosphorus/felt smoke on reproduction processes in rats, three studies were conducted: teratology, dominant lethal mutation, and reproduction in a single generation. Each of these studies was conducted at both the high- and intermediate-exposure levels and in the control (smoke-free) atmosphere.

At the high-dose level of each study, several of the animals died. Five of the 24 high-dose teratology females died before their scheduled necropsy date. Twelve of the 20 males for the single-generation study died prior to their time for mating. Nine of the 20 males for the dominant lethal mutation study died before they could be mated.

3.6.1 Teratology.

Pregnant females were exposed to test and control atmospheres from days 6 to 15 of gestation. There were no major abnormalities found among the control or test fetuses. The pregnancy rates for control, intermediate-dose and high-dose smoke were 100%, 100%, and 90%, respectively. Data on the number and condition of implants, the mean body weights of the fetuses, and the averaged data on implants appear in appendix B, table B-11. Statistical analysis of these data showed no differences between control and treatment groups.

3.6.2 Dominant lethal mutation.

In the dominant lethal mutation study, analysis by the chi-square method showed that, for the first mating, significantly more of the dams mated to intermediate-dose males had one or more resorptions as compared to the dams mated to control males, appendix B, table B-12. This difference was not observed at the high dose, indicating that the difference observed with the intermediate-dose group was probably not attributable to the effects of white phosphorus/felt smoke.

3.6.3 Single-generation reproduction.

The single-generation reproduction study results are more difficult to analyze. Although there were no significant differences in the body weights of the pups at birth, survivability of the exposed pups was significantly lower than that of the control pups, appendix B, table B-13. Exposures continued for the pups and dams through this 21-day period. Weight gain in the surviving exposed pups was less than that of the control pups, appendix B, table B-14. The difficulty arises from the inability to discern whether the deficiency in weight gain was (1) the result of the exposed dams not caring for their pups, (2) a decrease in mammary gland secretion, (3) the inability of the pups to nurse because of irritated and congested tracheas, or (4) exposure effects.

3.7 Physiological studies.

Physiological measurements were made on days 3 and 4 after the animals were removed from the exposure. The number of animals (sample size) used in the tests are shown in appendix B, tables B-15 and B-16.

An analysis of variance (ANOVA) was made on the data to determine the effect of dose (exposure level), sex difference, and the effect of dose within sexes. Following this, a T-test was performed to locate any significant differences.

The logic for determining a physiological effect from the white phosphorus/felt smoke required that the following conditions apply: (1) a significant difference at a $P \leq 0.05$ level be evidenced by the analysis of variance and Student T test, (2) the differences must be dose related and directional so that significant differences occurring in a low-dose group that were not reinforced by similar effects in the high-dose groups would be considered a chance occurrence, and (3) the difference should be time related unless an adaptive response for increased tolerance has developed. With a bioaccumulated material, it would be expected that effects shown after a 6-week exposure would be repeated after a 13-week exposure. With white phosphorus smoke, it is interesting to note from pathology (page 10) that upper airway irritation, i.e., tracheitis and laryngitis,

decreased after a 6-weeks' exposure. Assuming that phosphorous pentoxide unites with water lining the respiratory tract to form a phosphoric acid, the response to this irritant may be decreasing with time of exposure and consequently the application of present statistical judgments takes the possibility of increased tolerance into effect.

The results are shown in appendix B, tables B-15 through B-17. At both 6- and 13-weeks' exposure, significant sex differences were shown which appear to be related to the greater size of the male rats. These included breathing volumes and the increased inhaled volume responses to 6% CO₂. In addition, blood pressures from male rats were slightly higher than those of female rats. This has been observed in other tests.

Some differences appeared to be the effect of dose and these are indicated in tables B-15 and B-16. However, none of these effects satisfied the logic described above for determining a physiological effect. The same applies for the sex-related doses. It is noted that the sample size in the high-dose exposures was reduced because of deaths during the procedure. It is possible that, if the sample size were larger for high-dose groups, a statistical significance would have been noted. It appears that some effect was developing in the group toward a reduction in tidal volume and an increase in breathing frequency with dose in the 13-week exposed animals. There is also indication that there was less growth in the male rats of this group.

Table B-17 contains the qualitative or nonparametric observations made on rats in the exposure groups. Three of the 13-week high-exposure groups had loud bubbly rales 3 days after exposure which were absent on the fifth post-exposure day.

Although no statistical validation for a functional effect exists, the presence of rales and the tendency for a reduction in tidal volume and an increase in breathing frequency in the high-dose animals indicate that a careful examination of the lung pathology data and the pulmonary resistance data be made.

The evaluation of the pulmonary function as a result of exposure to white phosphorus/felt smoke was carried out on rats that had been exposed for a period of 13 weeks. The method for estimating the pulmonary resistance in these animals was based on a comparison of the plethysmographic pressure during a respiratory cycle and the peak respiratory flow. The rationale for using this method is based on the principle that the changes in pressure in a body plethysmograph during a respiratory cycle are proportional to the alveolar pressure during post cycle. (Pulmonary resistance is determined by the ratio of alveolar pressure to the flow rate during a respiratory cycle; therefore, an estimate of the resistance can be determined by substituting the plethysmographic pressure for the alveolar pressure.)

The results of the pulmonary tests in the unanesthetized rat following 13-weeks exposure to white phosphorus/felt smoke are presented in appendix B, table B-18. There were no significant differences from control values in the respiratory rate or peak inspiratory flow rates in either males or females exposed to smoke. There was no significant difference in the estimated pulmonary resistance of the female rats following exposure. The estimated pulmonary resistance of exposed male rats had a tendency to increase slightly over that of the controls. This increase was significantly different in the low-dose rats but not in the high-dose animals; however, the indication is that some pulmonary damage may be present in the male rats exposed to white phosphorus/felt smoke. No rats were tested at 6 weeks postexposure.

3.8 Behavioral studies.

The behavioral responses of rats exposed to white phosphorus smoke for 6 or 13 weeks was measured using spontaneous activity and passive avoidance tests. In all instances, values are compared statistically to a group of unexposed control rats of equal age and weight.

3.8.1 Spontaneous activity.

The results of these tests are presented in appendix B, table B-19, which shows the gross and fine activity of the rats and the ratio between these two types of activity. Both male and female animals exposed for 6 weeks appeared to exhibit a difference in activity; however, the mean values presented were influenced by one or two animals from each group including controls. If the ratio is calculated from these means, the values become more uniform, indicating that spontaneous activity was not altered as a result of exposure.

3.8.2 Passive avoidance.

Passive avoidance test results are presented in appendix B, table B-20. The exposed female rats, at 1161- and 589-mg/m³ dose levels and 6-week/13-week exposure time periods, were no different from control animals. This indicated that the animals' ability to passively avoid shocks was not adversely affected by exposure to white phosphorus smoke. Male rats exposed to the high dose received more shocks than the control rats but statistically the values were not significantly different. The number of passive avoidance responses were no different. One of the 13-week high-dose male rats received an unusually large number of shocks with no attempted avoidance, raising the mean value for this group of animals. This animal had either a higher pain threshold than the other animals or a delay in determining how to avoid the shock. The lower-dose male rats showed no differences from the control animals.

4. DISCUSSION

When white phosphorus burns, it forms a number of oxides of phosphorus which are rapidly converted by moisture to phosphorus and phosphonic acids.^{1,3} Although at ordinary expected field concentrations (100-200 mg/m³), this may not be hazardous, some irritation to the eyes, nose, and throat may occur.⁴ Cullumbine⁵ exposed a total of 108 men to white phosphorus smoke at concentrations from 87 to 1770 mg/m³. Throat irritation was produced at all concentrations. From these data, it has been estimated that the minimum harassing concentration (requiring a respirator) is about 700 mg/m³. In the documentation for threshold limit values (TLV), it has been reported that concentrations of 100 mg/m³ were unendurable except to hardened workers.⁶ A TLV of 1 mg/m³ was established as the level to which nearly all workers may be repeatedly exposed without adverse effect. A man exposed to 100 mg/m³ would probably mask or remove himself from the smoke cloud.⁷

In the study just completed, the 1000 mg/m³ dose, with 40% spontaneous deaths and injury to all other animals, was obviously a hazardous concentration. None of the animals exposed at the 500- or 200-mg/m³ dose levels died. The intermediate dose did, however, produce tracheitis in 50% of the rats. Only one of the low-dose animals showed any signs of irritation.

5. CONCLUSIONS

It would appear that the chance of injury is high at 1161 mg/m³ and low at 193 mg/m³. At 589 mg/m³, one-half of the rats showed some exposure effects.

The rats apparently developed a tolerance to repeated exposures, particularly at the lowest exposure level.

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APPENDIX A

CHEMICAL ANALYSIS OF WHITE PHOSPHORUS SMOKE*

Exposure chamber air samples received were diluted with distilled water, shaken, then boiled 10 minutes to convert the phosphorus acids to orthophosphoric acid, then cooled to room temperature. Sample volume was measured after boiling. Using a pH meter as an indicator, the acid content was determined by titration against 0.10043 N sodium hydroxide to a pH of 9.6. After measuring the amount of 0.10043 N sodium hydroxide required to adjust the sample pH to 9.6, the following formula was used to determine normality of the orthophosphoric acid:

$$1. N_{\text{sample}} \times V_{\text{sample}} = N_{\text{NaOH}} \times V_{\text{NaOH}}$$

N = Normality

V = Volume of sample in milliliters

The normality of the acid is multiplied by 32.66 (milligrams per milligram-equivalents of orthophosphoric acid).

$$2. \frac{\text{milligram equivalents}}{\text{milliliters}} \times \frac{32.66 \text{ milligrams}}{\text{milligram equivalents}} = \frac{\text{milligrams}}{\text{milliliters of orthophosphoric acid}}$$

(normality of sample)

$$3. \frac{\text{milligrams}}{\text{milliliters}} \times \text{milliliters} = \text{milligrams of orthophosphoric acid in sample}$$

* B. P. Pearce. Porton Technical Paper 154. The Stability of Red Phosphorus Compositions. June 1974. UNCLASSIFIED Paper.

APPENDIX B
DETAILS OF TOXICOLOGICAL EVALUATION

Table B-1. Inhalation Exposure Doses Produced by Burning Cubes of White Phosphorus/Felt

Cube weight	Average exposure concentration	Average daily 15-minute exposure Ct	Total cumulative exposure Ct
gm	mg/m ³	mg min/m ³	mg min/m ³
20	1161	17,415	1,097,151 (63 days)
10	589	8,833	556,480 (63 days)
3	192.5	2,887	178,991 (62 days)

Table B-2. Spontaneous Deaths in Rats Exposed to the High-Dose Concentration of White Phosphorus Smoke

Exposure day	Deaths		Cumulative exposure Ct
	Male	Female	
			mg min/m ³
4		1	54,225
5	1		69,225
9	1		143,975
10	1		158,820
11		2	176,340
12	1	3	194,790
13	1	1	210,960
14	2	1	225,120
16		1	251,925
23	2		376,260
24		1	397,650
25	1		420,330
26	1		441,300
27	1		460,545
29		1	499,560
34	1		588,045
47	1		813,021
54	1		936,820
57	1		995,426

Table B-3. Organ and Total Body Weights in Male Sprague-Dawley Rats After Repeated Exposures to White Phosphorus Smoke

Dose level	Exposure time	Number of animals	Total body		Heart		Lungs		Liver		Kidneys		Gonads	
			Mean	Standard error	Mean	Standard error	Mean	Standard error	Mean	Standard error	Mean	Standard error		
grams														
High	6	0	—	—	—	—	—	—	—	—	—	—	—	—
	13	6	373	19	1.62	0.23	3.32+	0.22	14.9	1.8	2.78++	0.16	3.47	0.11
	17+++	9	455	30	1.77	0.20	3.55	0.35	17.2	3.4	3.12	0.45	3.40	0.60
High control	6	3	382	26	1.50	0.14	3.60	0.14	18.2	1.4	2.93	0.47	3.67	0.41
	13	3	389	14	1.53	0.17	2.93	0.12	15.2	2.9	3.00	0.82	3.67	0.19
	17+++	6	417	46	1.57	0.14	3.32	0.42	16.0	2.3	2.93	0.44	3.37	0.14
Intermediate	6	6	374	20	1.47	0.24	3.32	0.56	16.3	1.2	2.67	0.28	3.47	0.26
	13	6	433	27	1.68	0.19	3.25	0.22	16.2	2.6	2.83	0.31	3.52	0.21
	17+++	12	461++	46	1.64	0.21	3.36	0.37	17.9	3.1	3.11	0.31	3.62	0.47
Intermediate control	6	3	368	15	1.37	0.09	3.07	0.09	15.4	0.8	2.93	0.26	3.27	0.20
	13	3	456	34	1.63	0.17	3.27	0.17	16.0	1.2	2.87	0.05	3.30	0.33
	17+++	6	509	32	1.77	0.12	4.23	0.82	19.5	3.6	3.52	0.36	3.02	1.36
Low	6	6	346	20	1.50	0.15	3.50	0.36	16.2	1.5	2.67	0.11	3.35	0.10
	13	6	422	18	1.43	0.20	3.30	0.36	15.9	1.5	2.75	0.21	3.45	0.18
	17+++	6	453	55	1.48	0.23	2.98++	0.38	17.8	2.5	2.78	0.35	3.48	0.37
Low control	6	3	338	53	1.43	0.17	3.35	0.15	15.3	3.4	2.73	0.33	3.13	0.40
	13	3	444	63	1.53	0.19	3.43	0.25	18.8	2.8	3.00	0.29	3.63	0.25
	17+++	3	484	11	1.90	0.24	3.43	0.12	18.5	3.0	3.30	0.24	3.57	0.17

+ - Significantly higher than control based on statistical "t" test.

++ - Significantly lower than control based on statistical "t" test.

+++ - Four weeks' postexposure.

Table B-4. Organ and Total Body Weights in Female Sprague-Dawley Rats After Repeated Exposures to White Phosphorus Smoke

Dose level	Exposure time weeks	Number of animals	Total body		Heart		Lungs		Liver		Kidneys		Gonads	
			Mean	Standard error	Mean	Standard error	Mean	Standard error	Mean	Standard error	Mean	Standard error	Mean	Standard error
High	6	6	241	12	0.93	0.09	2.63+	0.38	9.0	0.6	1.65	0.13	0.200	0.082
	13	6	241	19	1.15	0.10	2.67	0.41	9.4	1.9	1.82	0.31	0.183	0.037
	17	7	255	16	1.06	0.14	2.76	0.57	10.1	0.7	1.79	0.16	0.143	0.050
High control	6	3	235	9	0.97	0.05	2.10	0.08	10.0	0.5	1.70	0.08	0.167	0.047
	13	3	270	12	1.10	0.14	2.43	0.19	9.4	1.2	1.87	0.12	0.200	-
	17	6	254	19	1.07	0.09	2.32	0.26	10.0	1.8	1.75	0.24	0.167	0.047
Intermediate	6	6	247	22	0.97	0.09	2.47	0.24	9.7	1.2	1.85	0.30	0.183	0.037
	13	6	269	21	1.20	0.13	2.75	0.25	10.3	1.1	1.90	0.21	0.200	0.037
	17	12	266	24	0.99++	0.10	2.41	0.18	9.4++	1.2	1.89++	0.18	0.150	0.050
Intermediate control	6	3	246	6	1.03	0.04	2.43	0.09	10.0	0.4	1.70	0.08	0.167	0.04
	13	3	260	28	1.17	0.12	2.50	0.08	9.9	0.6	1.83	0.09	0.200	-
	17	6	275	13	1.15	0.08	2.33	0.12	10.8	1.1	2.15	0.19	0.150	0.05
Low	6	6	232	16	1.08	0.11	2.48	0.23	9.8	1.2	1.90	0.20	0.167	0.047
	13	6	240	15	1.05	0.13	2.33	0.09	8.8	0.9	1.83	0.17	0.167	0.047
	17	6	287	23	1.08	0.11	2.45	0.13	10.7	1.4	1.98	0.15	0.183+	0.037
Low control	6	3	229	24	1.07	0.17	2.47	0.45	8.9	1.4	1.90	0.16	0.200	0.08
	13	3	243	20	1.07	0.05	2.37	0.05	9.3	0.8	1.93	0.20	0.233	0.05
	17	2	270	5	1.25	0.05	2.35	0.15	9.9	-	2.65	0.35	0.100	-

+ - Significantly higher than control based on statistical "t" test.

++ - Significantly lower than control based on statistical "t" test.

Table B-5. Hematology in Rats Exposed for Six Weeks to White Phosphorus Smoke

Cumulative exposure Ct	Red blood cells			White blood cells			Hematocrit			Hemoglobin			Neutrophils		
	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation
		$\times 10^6/\text{mm}^3$	$\times 10^6/\text{mm}^3$		per mm^3	per mm^3		%	%		mg/100 ml	mg/100 ml		%	%
mg min/m ³	6	6.32	0.77	6	8333.33	1129.40	6	35.70	4.46	6	13.53	1.59	-	-	-
499,560	6	6.90	0.58	6	9650.00	1698.77	6	38.53	2.95	6	15.10	0.87	-	-	-
Control	12	7.02	0.53	12	6633.33	1818.12	12	39.11	3.34	12	14.42	0.94	12	7.42	5.63
246,285	6	6.90	0.34	6	5966.67	1188.37	6	38.10	2.19	6	14.18	0.84	6	7.00	4.16
Control	12	6.50	0.54	12	8325.00	1799.13	12	35.68	3.08	12	13.51	0.94	12	8.92	5.25
84,019	6	6.95	0.41	6	10233.33	1569.15	6	38.58	2.10	6	14.68	0.71	6	10.17	3.80
Control	6														

Cumulative exposure Ct	Band cells			Lymphocytes			Mono cytes			Eosinophils			Basophils		
	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation
		%	%		%	%		%	%		%	%		%	%
mg min/m ³	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
499,560	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Control	12	91.50	5.06	12	92.67	4.57	12	1.00	0.00	6	2.17	1.67	-	-	-
246,285	6	90.25	5.55	6	90.25	5.55	6	1.00	0.00	1	1.50	0.76	-	-	-
Control	12	88.00	4.93	12	88.00	4.93	12	2.00	0.82	2	2.00	1.00	-	-	-
84,019	1	1.00	0.00	6											
Control	1														

+ Significantly lower than control based on statistical "t" test.

NOTE: Statistical evaluation of differential white count components, monocytes, eosinophils, basophils and band cells may be meaningless since normal occurrences range from 1% to 10%.

Table B-6. Hematology in Rats Exposed for Thirteen Weeks to White Phosphorus Smoke

Cumulative exposure Ct	Red blood cells			White blood cells			Hematocrit			Hemoglobin			Neutrophils		
	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation
		$\times 10^6/\text{mm}^3$	$\times 10^6/\text{mm}^3$		per mm^3	per mm^3		%	%		mg/100 ml	mg/100 ml		%	%
mg min/m ³															
1,097,151	12	7.32*	0.59	12	15,125.00	5301.47	12	40.12*	3.40	12	15.43*	1.28	10	31.10**	12.04
Control	6	8.12	0.46	6	14,350.00	3114.35	6	44.83	1.64	6	17.48	0.77	6	15.00	6.53
556,480	12	7.13	0.41	12	7691.67*	607.53	12	39.05	2.26	12	14.77	0.77	12	15.67	12.47
Control	6	7.38	0.68	6	8633.33	727.25	6	39.47*	3.16	6	15.10	1.23	4	11.00	8.77
178,991	12	7.04**	0.88	12	9533.33	2489.76	12	38.51*	4.63	12	13.95**	1.90	12	14.58	4.61
Control	6	5.46	1.05	6	8416.67	2625.15	6	29.88	6.50	6	10.98	2.00	6	10.67	4.85

Cumulative exposure Ct	Band cells			Lymphocytes			Monocytes			Eosinophils			Basophils		
	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation
		%	%		%	%		%	%		%	%		%	%
mg min/m ³															
1,097,151	-	-	-	10	66.70	13.10	1	1.00	0.00	6	3.50	1.38	-	-	-
Control	-	-	-	6	84.33	7.23	-	-	-	2	2.00	1.00	-	-	-
556,480	-	-	-	12	83.67	12.39	-	-	-	3	2.67	0.94	-	-	-
Control	-	-	-	4	88.50	8.99	-	-	-	1	2.00	0.00	-	-	-
178,991	-	-	-	12	84.67	4.48	3	1.33	0.47	4	1.25	0.43	-	-	-
Control	-	-	-	6	88.83	4.78	-	-	-	2	1.50	0.50	-	-	-

Table B-7. Hematology in Rats 30 Days After 13 Weeks' Exposure to White Phosphorus Smoke

Cumulative exposure Ct	Red blood cells			White blood cells			Hematocrit			Hemoglobin			Neutrophils		
	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation
mg min/m ³		$\times 10^6/\text{mm}^3$	$\times 10^6/\text{mm}^3$		per mm ³	%		%	%		mg/100 ml	mg/100 ml		%	%
1,097,151 control	16	7.15	1.0	16	11,506.25*	1747.31	16	40.81	4.55	16	14.48	1.07	16	33.44*	16.56
556,480 control	12	7.29	0.71	12	9558.33	2457.80	12	39.31	4.44	12	14.45	1.84	12	20.08	11.16
178,991 control	24	7.07	0.57	24	8854.17	1918.55	24	38.57	3.00	24	14.44	0.99	24	11.17	6.38
	12	7.47	0.43	12	9575.00	2876.09	12	44.06	2.39	12	15.02	0.92	12	13.92	5.12
	12	6.67	0.93	12	10,918.13	1141.97	12	37.74	4.94	12	14.96	1.86	12	12.42	5.33
	5	6.61	0.70	5	11,600.00	1404.28	5	36.96	3.91	5	14.74	1.22	5	12.90	6.60

Cumulative exposure Ct	Band cells			Lymphocytes			Monocytes			Eosinophils			Basophils		
	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation
mg min/m ³		%	%		%	%		%	%		%	%		%	%
1,097,151 control	16	65.75	16.74	2	1.00	0.00	4	2.75	0.83	4	2.75	0.83	-	-	-
556,480 control	12	78.67	11.01	3	1.00	0.00	7	1.57	0.73	7	1.57	0.73	-	-	-
178,991 control	24	88.04	6.26	1	4.00	0.00	13	1.15	0.36	13	1.15	0.36	-	-	-
	12	85.58	5.19	-	-	-	5	1.20	0.40	5	1.20	0.40	-	-	-
	12	87.00	4.93	-	-	-	4	1.75	0.83	4	1.75	0.83	-	-	-
	5	87.20	6.52	-	-	-	3	1.33	0.47	3	1.33	0.47	-	-	-

* Significantly higher than control based on statistical "t" test.

++ Significantly lower than control based on statistical "t" test.

NOTE: Statistical evaluation of differential-white count components, monocytes, eosinophils, basophils, and band cells may be meaningless since normal occurrences range from 1% to 10%.

Table B-8. Blood Chemistry in Rats Five Weeks' Exposure to White Phosphorus Smoke

Cumulative exposure Ct	Glucose			Blood urea nitrogen			Creatinine			Sodium			Potassium		
	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation
mg min/m ³		mg/dl			mg/dl			mg/dl			mg/dl			mg/dl	
499,560	6	150.17*	12.40	6	23.00	3.06	6	0.70	0.08	6	145.17	1.77	6	4.43	0.55
Control	6	187.17	30.10	6	22.83	2.97	6	0.63	0.09	6	145.50	2.36	6	4.97	1.02
246,285	12	165.83	15.46	12	21.33	1.84	12	0.54	0.12	12	146.58	1.38	12	4.52	0.51
Control	6	171.67	15.88	6	23.83	2.97	6	0.65	0.17	6	147.33	3.25	6	4.47	0.86
84,019	11	181.18**	22.39	11	20.64	2.38	11	0.55	0.08	11	145.27	2.18	11	4.25	0.86
Control	6	159.17	8.03	6	19.33	0.75	6	0.50	0.10	6	145.83	1.21	6	4.05	0.35

Cumulative exposure Ct	Chloride			Carbon dioxide			Uric acid			Total protein			Albumin		
	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation
mg min/m ³		meq/l			meq/l			mg/dl			mg/dl			mg/dl	
499,560	6	103.33	1.11	6	21.67	4.31	6	0.85	0.68	6	5.58	0.42	6	3.03	0.32
Control	6	101.67	1.37	6	22.00	3.83	6	1.37	1.09	6	6.07	0.23	6	3.30	0.15
246,285	12	102.92	2.36	12	22.33	2.39	12	1.32	0.78	12	6.17	0.22	12	3.23	0.12
Control	6	102.87	2.13	6	23.50	4.19	6	1.48	0.84	6	6.05	0.26	6	3.18	0.15
84,019	11	103.55	2.23	11	19.09	5.81	11	1.47	1.37	11	5.54	0.53	11	2.76	0.46
Control	6	104.90	7.00	6	22.00	4.62	6	0.73	0.25	6	5.87	0.43	6	3.15	0.24

Cumulative exposure Ct	Globulin			Calcium			Phosphate			Cholesterol			Triglycerides		
	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation
mg min/m ³		gm/dl			gm/dl			mg/dl			mg/dl			mg/dl	
499,560	6	2.55	0.28	6	9.77	0.57	6	4.93*	0.65	6	75.00	6.11	6	33.67*	16.60
Control	6	2.77	0.14	6	10.25	0.43	6	6.07	0.51	6	78.50	11.77	6	59.83	23.02
246,285	12	2.73	0.16	12	9.79	0.36	12	5.93	0.54	12	73.17*	5.98	12	53.58	39.28
Control	6	2.87	0.14	6	9.65	0.17	6	5.90	0.75	6	79.67	4.31	6	89.00	46.53
84,019	11	2.57	0.18	11	9.67	0.33	11	5.95	1.13	11	106.18	23.92	11	49.91	32.24
Control	6	2.72	0.27	6	9.87	0.25	6	6.15	0.52	6	97.67	9.84	6	51.83	24.13

Cumulative exposure Ct	Alkaline phosphatase			Glutamic oxalacetic transaminase			Glutamic pyruvic transaminase			Lactic dehydrogenase			Total bilirubin		
	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation
mg min/m ³		u/l			u/l			u/l			u/l			mg/dl	
499,560	6	230.50	51.19	6	147.33	90.76	6	57.33	14.01	6	382.17	297.98	6	0.10	0.00
Control	6	335.83	99.78	6	119.83	25.47	6	67.67	9.50	6	322.67	88.68	6	0.10	0.00
246,285	12	366.17	139.84	12	120.83	54.22	12	53.08	16.85	12	287.50	173.36	12	0.32	0.39
Control	6	301.00	96.19	6	140.00	81.76	6	59.17	21.99	6	1472.17	2696.11	6	0.10	0.00
84,019	11	355.09	90.90	11	126.18	44.53	11	55.09	10.72	11	342.27	173.08	11	0.10	0.00
Control	6	306.60	105.04	6	117.50	53.59	6	49.00	9.45	6	265.67	43.60	6	0.10	0.00

* Significantly lower than control based on statistical "t" test.
 ** Significantly lower than control based on statistical "t" test.

Table B-9. Blood Chemistry in Rats Bled After 13 Weeks Exposure to White Phosphorus Smoke

Cumulative exposure Ct	Glucose			Blood urea nitrogen			Creatinine			Sodium			Potassium		
	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation
mg min/m ³		mg/dl	mg/dl		mg/dl	mg/dl		mg/dl	mg/dl		meq/l	meq/l		meq/l	meq/l
499,560	12	178.58	22.76	12	20.58	4.33	12	0.57	0.07	12	146.61	2.05	12	4.43	0.65
Control	6	168.83	17.35	6	17.50	1.71	6	0.53	0.05	6	147.17	0.69	6	4.28	0.38
246,285	12	166.50	12.27	12	20.33	3.09	12	0.57	0.11	12	144.33	1.60	12	4.07	0.22
Control	6	174.50	14.85	6	21.33	3.14	6	0.63	0.5	6	144.56	0.96	6	4.20	0.68
84,019	12	171.00*	16.87	12	21.67	1.49	12	0.52	0.09	12	145.92	0.86	12	4.18	0.43
Control	6	187.17	7.45	6	23.00	2.58	6	0.57	0.05	6	145.50	0.96	6	4.27	0.36

Cumulative exposure Ct	Chloride			Carbon dioxide			Uric acid			Total protein			Albumin		
	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation
mg min/m ³		meq/l	meq/l		meq/l	meq/l		mg/dl	mg/dl		gm/dl	gm/dl		gm/dl	gm/dl
499,560	12	106.00	2.68	12	17.58	4.31	12	1.33	1.38	12	5.85	0.27	12	3.30	0.22
Control	6	107.50	0.50	6	17.50	1.71	6	1.05	0.81	6	5.75	0.32	6	3.30	0.14
246,285	12	104.92	2.20	12	19.83	3.13	12	1.23	0.40	12	5.78	0.20	12	3.18	0.11
Control	6	104.67	3.45	6	21.17	3.18	6	1.18	0.64	6	5.90	0.19	6	3.33	0.09
84,019	12	103.56	1.85	12	19.42	2.90	12	0.86	1.13	12	5.80	0.20	12	3.19	0.13
Control	6	104.33	1.97	6	19.00	2.89	6	1.08	0.41	6	5.83	0.25	6	3.10	0.16

Cumulative exposure Ct	Globulin			Calcium			Phosphate			Cholesterol			Triglycerides		
	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation
mg min/m ³		gm/dl	gm/dl		gm/dl	gm/dl		mg/dl	mg/dl		mg/dl	mg/dl		mg/dl	mg/dl
499,560	12	2.55	0.13	12	9.68	0.57	12	4.92	1.09	12	111.42	30.22	12	36.25	24.69
Control	6	2.45	0.24	6	9.70	0.24	6	5.08	0.76	6	123.83	12.35	6	57.67	21.01
246,285	12	2.60	0.15	12	9.37	0.23	12	4.70	0.45	12	74.25	9.69	12	31.33	33.24
Control	6	2.57	0.11	6	9.55	0.29	6	5.07	0.53	6	74.33	11.01	6	21.50	20.95
84,019	12	2.61	0.13	12	9.67	0.20	12	5.01	0.52	12	77.92	8.62	12	37.42	24.68
Control	6	2.73	0.19	6	9.43	0.30	6	5.02	0.39	6	77.33	6.05	6	20.67	18.12

Cumulative exposure Ct	Alkaline phosphatase			Glutamic oxalacetic transaminase			Glutamic pyruvic transaminase			Lactic dehydrogenase			Total bilirubin		
	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation
mg min/m ³		u/l	u/l		u/l	u/l		u/l	u/l		u/l	u/l		mg/dl	mg/dl
499,560	12	352.58**	103.00	12	109.08	37.23	12	55.17	13.40	12	290.00	168.56	12	0.10	0.00
Control	6	270.50	48.41	6	85.33	16.36	6	47.17	7.06	6	258.83	85.31	6	0.10	0.00
246,285	12	262.00	72.63	12	91.67	38.87	12	45.75	10.30	12	290.50	117.40	12	0.16	0.05
Control	6	247.67	49.52	6	80.33	9.29	6	40.17	6.12	6	221.33	64.50	6	0.15	0.05
84,019	12	287.42	101.75	12	108.50	30.82	12	58.92	20.54	12	253.67	49.95	12	0.11	0.03
Control	6	295.50	86.50	6	133.67	53.31	6	66.50	15.02	6	411.00	203.72	6	0.12	0.04

* Significantly lower than control based on statistical "t" test.
 ** Significantly higher than control based on statistical "t" test.

Table B-10. Blood Chemistry in Pigs Fed 4 Weeks After a 13-week Exposure to White Phosphorus Smoke

Cumulative exposure Ct	Glucose			Blood urea nitrogen			Creatinine			Sodium			Potassium		
	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation
mg min/m ³		mg/dl	mg/dl		mg/dl	mg/dl		mg/dl	mg/dl		meq/l	meq/l		meq/l	meq/l
499,560	16	173.81	12.53	16	22.25	2.22	16	0.72	0.09	16	147.19*	1.78	16	4.13	0.28
Control	12	175.17	20.32	12	22.67	3.77	12	0.69	0.08	12	145.92	1.04	12	4.08	0.26
246,285	24	180.21	27.87	24	20.04*	1.84	24	0.57	0.07	24	146.42	3.45	24	4.17	0.66
Control	12	168.08	15.26	12	21.58	1.32	12	0.59	0.13	12	147.50	1.55	12	4.05	0.26
84,019	12	196.75	26.54	12	20.33	1.31	12	0.53	0.06	12	145.58	1.66	12	4.31	0.67
Control	5	189.80	20.71	5	18.80	1.17	5	0.56	0.12	5	144.60	1.62	5	4.56	0.69

Cumulative exposure Ct	Chloride			Carbon dioxide			Uric acid			Total protein			Albumin		
	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation
mg min/m ³		meq/l	meq/l		meq/l	meq/l		mg/dl	mg/dl		gm/dl	gm/dl		gm/dl	gm/dl
499,560	16	105.56	1.37	16	19.31	2.52	16	0.98	0.39	16	5.86	0.25	16	3.27	0.18
Control	12	105.43	2.37	12	21.17	2.82	12	1.02	0.70	12	5.92	0.33	12	3.32	0.27
246,285	24	103.42	2.18	24	20.92	2.71	24	1.01	0.67	24	5.64**	0.29	24	3.17**	0.17
Control	12	104.00	2.61	12	20.00	3.46	12	0.76	0.25	12	6.07	0.29	12	3.39	0.22
84,019	12	103.25	1.69	12	25.08	2.25	12	1.35	1.10	12	6.06	0.35	12	3.38	0.12
Control	5	103.40	0.49	5	24.80	0.75	5	1.16	0.83	5	5.88	0.43	5	3.28	0.24

Cumulative exposure Ct	Globulin			Calcium			Phosphate			Cholesterol			Triglycerides		
	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation
mg min/m ³		gm/dl	gm/dl		gm/dl	gm/dl		mg/dl	mg/dl		mg/dl	mg/dl		mg/dl	mg/dl
499,560	16	2.58	0.19	16	9.41	0.27	16	4.69	0.63	16	79.37	18.26	16	49.62	34.81
Control	12	2.59	0.11	12	9.42	0.49	12	4.32	0.81	12	78.33	19.72	12	54.00	34.45
246,285	24	2.47**	0.20	24	9.56	0.54	24	5.17	0.59	24	74.83**	6.54	24	65.92	52.12
Control	12	2.67	0.12	12	9.75	0.42	12	5.01	0.67	12	84.75	13.55	12	94.83	65.87
84,019	12	2.67	0.19	12	10.10	0.24	12	5.33	0.56	12	74.25	9.44	12	56.73	32.14
Control	5	2.60	0.28	5	9.98	0.55	5	5.36	0.33	5	75.60	9.41	5	48.80	16.44

Cumulative exposure Ct	Alkaline phosphatase			Glutamic oxalacetic transaminase			Glutamic pyruvic transaminase			Lactic dehydrogenase			Total bilirubin		
	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation	No. of animals	Mean	Standard deviation
mg min/m ³		u/l	u/l		u/l	u/l		u/l	u/l		u/l	u/l		mg/dl	mg/dl
499,560	16	274.69	69.42	16	91.62	26.71	16	48.62	13.72	16	278.06	113.32	16	0.10	0.00
Control	12	299.83	102.99	12	97.83	21.56	12	56.25	11.36	12	305.67	76.71	12	0.10	0.00
246,285	24	262.33	75.80	24	107.92	41.29	24	57.08	25.54	24	321.08	109.66	24	0.10	0.00
Control	12	304.92	84.19	12	110.92	38.15	12	69.50	21.80	12	315.92	61.94	12	0.10	0.00
84,019	12	293.75	90.84	12	126.08	90.45	12	80.00	57.57	12	246.92	84.23	12	0.25	0.14
Control	5	218.00	60.98	5	93.40	17.45	5	58.40	11.57	5	255.80	85.11	5	0.10	0.00

* Significantly lower than control based on statistical "t" test.

** Significantly higher than control based on statistical "t" test.

	Air controls	Dose level 589 mg/m ³	1,161 mg/m ³
Number pregnant	20	20	18
Percent pregnant	100	100	90
Total implants	238	242	221
Live implants	225	236	206
Dead implants	13	6	15
Percent dead implants	5.46	2.48	6.79
Mean weight in grams			
Male			
Female	3.91 ± 0.32	3.83 ± 0.36	3.87 ± 0.38
Mean body weight - all pups	3.76 ± 0.34	3.67 ± 0.30	3.66 ± 0.40
Average implants per pregnant female	3.84 ± 0.33	3.76 ± 0.34	3.77 ± 0.40
Average live implants per pregnant female	11.90 ± 1.45	12.10 ± 1.37	12.28 ± 1.96
Average dead implants per pregnant female	11.25 ± 1.41	11.80 ± 1.61	11.44 ± 2.28
	0.65 ± 0.67	0.30 ± 0.57	0.83 ± 1.10

Table B-12. Reproductive Data for Female Rats Mated to Males Exposed to White Phosphorus/Smoke
(Numbers in parentheses indicate the number of animals in each category.)

Group	Week	Number mated	Number pregnant	M.I.*	C.L.I.	I.I.	P.I.I.I.	F.I.	R.I.	N.V.F./V.F.	N.V.F.≥1	N.V.F.≥2
Air control	1	20	14	70	(183) 13.07	(165) 11.79	(18) 1.29	(158) 11.29	(7) 0.50	7/158	5/9	2/12
	2	20	19	95	(253) 13.32	(238) 12.53	(15) 0.79	(223) 11.74	(15) 0.79	15/223	9/10	4/15
589 ₃ mg/m ³	1	20	19	95	(257) 13.53	(224) 11.79	(33) 1.74	(210) 11.05	(14) 0.74*	14/210	13/6	1/18
	2	20	20	100	(278) 13.90	(259) 12.95	(19) 0.95	(249) 12.45	(10) 0.50	10/249	7/13	3/17
1161 ₃ mg/m ³	1	20	18	90	(256) 14.22	(226) 12.56	(30) 1.67	(215) 11.94	(11) 0.61	11/215	8/10	2/16
	2	20	18	90	(255) 14.17	(219) 12.17	(36) 2.00	(215) 11.94	(4) 0.22	4/215	4/14	0/18

*Abbreviations used

M.I. (mating index) = $\frac{\text{total number of females pregnant} \times 100}{\text{total number of females mated}}$

C.L.I. (corpus luteus index) = $\frac{\text{total number of corpus lutea}}{\text{total number of pregnant females}}$

I.I. (implantation index) = $\frac{\text{total number of implantation sites}}{\text{total number of pregnant females}}$

P.I.I. (pre-implantation loss index) = $\frac{\text{total number of corpus lutea} - \text{total number of implantation sites}}{\text{total number of pregnant females}}$

F.I. (fetal index) = $\frac{\text{total number of viable fetuses}}{\text{total number of pregnant females}}$

R.I. (resorption index) = $\frac{\text{total number of deaths (early and late)}}{\text{total number of pregnant females}}$

N.V.F./V.F. = $\frac{\text{total number of resorptions}}{\text{total number of viable fetuses}}$

N.V.F. ≥ 1 = $\frac{\text{total number of females with one or more resorptions}}{\text{total number of females with zero resorptions}}$

N.V.F. ≥ 2 = $\frac{\text{total number of females with two or more resorptions}}{\text{total number of females with one or zero resorptions}}$

*Significant at $p < 0.05$

Table B-13. Viability, Survival, and Lactation Indices in a Single-Generation Study of Reproduction Performance During Exposure to White Phosphorous/Felt Smoke

Index	Generation	Control	Low dose *	High dose **
Viability index	F1	99.48	93.23	64.12
Survival index: day 21	F1	98.44	92.19	30.23
Lactation index	F1	98.95	98.88	47.15

* Low dose animals exposed to 589 mg/m³ white phosphorous/felt smoke.

** High dose animals exposed to 1,161 mg/m³ white phosphorous/felt smoke.

Table B-14. Single-Generation Reproduction Study of White Phosphorus in Cigarette Smoke

Days post-natal	Weight change (mean and SD)					
	Males			Females		
	Control	Low dose*	High dose**	Control	Low dose*	High dose**
1	(103) 6.63 ± 0.57	(90) 7.26 ± 0.74	(136) 6.38 ± 0.62	(89) 6.49 ± 0.69	(102) 6.76 ± 0.75	(166) 6.01 ± 0.69
4	(102) 10.41 ± 1.27	(84) 11.30 ± 1.15	(92) 9.41 ± 1.48	(89) 10.39 ± 1.54	(95) 10.71 ± 1.19	(101) 8.99 ± 1.59
7	(102) 15.36 ± 2.18	(84) 16.66 ± 1.67	(84) 13.97 ± 1.86	(89) 15.45 ± 2.69	(95) 15.64 ± 1.75	(90) 13.62 ± 2.26
14	(100) 29.59 ± 4.19	(83) 31.39 ± 3.52	(47) 26.46 ± 5.03	(89) 29.97 ± 5.31	(94) 29.46 ± 2.72	(44) 25.93 ± 5.53
21	(100) 45.05 ± 8.16	(83) 50.62 ± 5.34	(47) 41.10 ± 9.52	(89) 45.16 ± 9.71	(94) 46.55 ± 5.09	(44) 41.50 ± 11.15

* Low dose, 589 mg/m³.

** High dose, 1,161 mg/m³.

Table B-3. Physiological Effects of White Phosphorus Test Solution Pairs After 4 Weeks Exposure

ANOVA																		
Measurements	Units	Control						Exposure						Significance of F Ratio				
		All			Males			Low-dose			High-dose			Dose	Significance of F Ratio		Dose: female	
		n	Mean	SE	n	Mean	SE	All	Males	Females	All	Males	Females		Dose: male	Dose: female		
Sample size		12			6			22	6		6	6						
Weight	grams	317 ± 54	36.5	10	259 ± 25	32.7	78	385 ± 44	248 ± 12	360 ± 54	34.7 ± 10	252 ± 25			0.001			
Temperature rectal	°C	37.0 ± 0.4	100.1	0.3	37.0 ± 0.2	100.2	0.2	100.2 ± 0.2	100.2 ± 0.2	100.2 ± 0.2	100.2 ± 0.2	100.2 ± 0.2			0.01			0.01
Tidal volume	ml	1.75 ± .34	1.96	.12	1.55 ± .27	1.36	.20	2.05 ± .34	1.44 ± .27	1.68 ± .18	1.82 ± .08	1.53 ± .10			0.001			
Minute volume	ml	2.68 ± .47	205	.22	1.71 ± .47	206	.37	2.68 ± .26	1.72 ± .27	1.80 ± .45	2.15 ± .28	1.44 ± .19						
Breathing frequency	breaths per minute	107 ± 17	2.06	2.1	108 ± 24	1.03	.17	112 ± 14	95 ± .17	106 ± 17	1.18 ± .11	94 ± .11						
Tidal volume per CO ₂	ml	2.91 ± .40	3.07	.28	2.75 ± .46	3.15	.65	3.57 ± .45	2.63 ± .15	2.50 ± .42	3.26 ± .18	2.55 ± .14			0.001			0.05
Minute volume per CO ₂	ml	409 ± 105	451	.92	366 ± 127	403	.131	548 ± 59	362 ± .99	418 ± .97	505 ± .27	331 ± .92						
Breathing frequency per CO ₂	breaths per minute	119 ± 23	1.46	.24	132 ± 24	1.45	.19	153 ± 1.2	1.36 ± .12	143 ± .17	1.55 ± .12	113 ± .16			0.05			
Blood pressure, systolic	mm Hg	118 ± 5	122	.4	116 ± 5	120	.12	126 ± 11	114 ± .11	115 ± .10	116 ± .12	113 ± .10			0.05			
Heart rate from blood pressure	beats/min	413 ± 61	431	.60	395 ± 51	378	.39	397 ± 33	359 ± .37	317 ± .35	357 ± .26	394 ± .17						
Heart rate from ECG	beats/min	459 ± 49	465	.53	450 ± 48	464	.46	516 ± 107	451 ± .42	397 ± .46	396 ± .46	399 ± .56		0.01				0.01
ECG P-wave amplitude	mV	0.87 ± 0.23	0.87	.030	0.87 ± 0.30	0.87	.031	0.87 ± 0.30	0.87 ± 0.30	0.87 ± 0.30	0.87 ± 0.30	0.87 ± 0.30						
P-R interval	sec	0.17 ± 0.02	0.17	.002	0.17 ± 0.01	0.17	.002	0.17 ± 0.01	0.17 ± 0.01	0.17 ± 0.01	0.17 ± 0.01	0.17 ± 0.01						
Q-R interval	sec	0.24 ± 0.02	0.24	.002	0.24 ± 0.02	0.24	.002	0.24 ± 0.02	0.24 ± 0.02	0.24 ± 0.02	0.24 ± 0.02	0.24 ± 0.02						
Q-S interval	sec	0.39 ± 0.09	0.39	.008	0.39 ± 0.08	0.39	.007	0.39 ± 0.08	0.39 ± 0.08	0.39 ± 0.08	0.39 ± 0.08	0.39 ± 0.08			0.01			0.05
T-wave amplitude	mV	0.32 ± .15	.35	.10	0.32 ± .15	.35	.10	0.32 ± .15	0.32 ± .15	0.32 ± .15	0.32 ± .15	0.32 ± .15						
Treadmill run	min	12.5 ± 3.0	11.5	3.0	12.5 ± 3.0	11.5	3.0	12.5 ± 3.0	11.5 ± 3.0	11.5 ± 3.0	11.5 ± 3.0	11.5 ± 3.0						

* Values indicate standard deviation.

* Student's "t" test - different from control at P < 0.05.

Table B-16. Physiological Effects of White Phosphorus/Felt Smoke on Rats After 13 Weeks' Exposure

Measurement	Units	Control						Exposure						ANOVA			
		All			Males			Females			All			High-dose			Significance of F ratio (A)
		12	6	3	6	3	6	6	3	6	12	6	3	7	4	3	
Sample size		12	6	3	6	3	6	6	3	6	12	6	3	7	4	3	
Weight	grams	365 ± 43	441 ± 16	268 ± 28	358 ± 103	458 ± 39	257 ± 19	328 ± 78	348 ± 78	99.7 ± 0.21	99.6 ± 0.28	99.7 ± 0.21	99.6 ± 0.40 ^{**}	0.01	0.05	0.05	
Temperature, rectal	degrees F	99.9 ± .54	99.9 ± .77	100.0 ± .17	100.8 ± .94 ^{**}	100.1 ± .60	101.5 ± .68 ^{**}	101.5 ± .68 ^{**}	101.5 ± .68 ^{**}	1.91 ± .17 ^{**}	1.86 ± .28	1.91 ± .17 ^{**}	1.79 ± .43	0.05	0.05	0.05	
Tidal volume	ml	2.20 ± .39	2.51 ± .25	1.89 ± .22	1.78 ± .37 ^{**}	2.06 ± .31 ^{**}	1.50 ± .12 [*]	1.50 ± .12 [*]	1.50 ± .12 [*]	2.15 ± .28	2.15 ± .28	2.15 ± .28	2.07 ± .42	0.05	0.05	0.05	
Minute volume	ml	215 ± 62	264 ± 43	166 ± 30	185 ± 30	196 ± 34	174 ± 24	174 ± 24	174 ± 24	221 ± 16	221 ± 16	221 ± 16	207 ± 42	0.05	0.05	0.05	
Breathing frequency	breaths per minute	97 ± 18	105 ± 12	88 ± 18	106 ± 17	95 ± 16	116 ± 11	116 ± 11	116 ± 11	117 ± 14 ^{**}	117 ± 14 ^{**}	117 ± 14 ^{**}	117 ± 13	0.01	0.05	0.05	
Tidal volume, 6% CO ₂	ml	3.14 ± .48	3.50 ± .31	2.78 ± .31	2.80 ± .52	3.21 ± .37	2.39 ± .21	2.39 ± .21	2.39 ± .21	3.06 ± .38	3.06 ± .38	3.17 ± .35	2.91 ± .43	0.001	0.05	0.05	
Minute volume, 6% CO ₂	ml	410 ± 93	467 ± 106	371 ± 46	388 ± 60	419 ± 47	358 ± 50	358 ± 50	358 ± 50	428 ± 83	428 ± 83	470 ± 85	373 ± 41	0.01	0.05	0.05	
Breathing frequency, 6% CO ₂	b/min	133 ± 22	133 ± 28	134 ± 16	141 ± 20	132 ± 23	149 ± 14	149 ± 14	149 ± 14	140 ± 21	140 ± 21	140 ± 21	129 ± 13				
Blood pressure, systolic	mm Hg	119 ± 6.0	122 ± 7.1	117 ± 3.2	119 ± 7.6	123 ± 6.3	115 ± 6.4	115 ± 6.4	115 ± 6.4	119 ± 6.1	119 ± 6.1	121 ± 7.6	117 ± 3.6				
Heart rate (from blood pressure)	b/min	389 ± 30	383 ± 29	394 ± 33	456 ± 30 [*]	445 ± 34 [*]	467 ± 44 [*]	467 ± 44 [*]	467 ± 44 [*]	418 ± 29	418 ± 29	417 ± 21	420 ± 44	.001	0.05	0.05	
Heart rate (from ECG)	b/min	439 ± 41	432 ± 44	445 ± 39	474 ± 44	464 ± 28	484 ± 57	484 ± 57	484 ± 57	459 ± 46	459 ± 46	440 ± 53	486 ± 16				
ECG - P-wave amplitude	mV	.055 ± .016	.060 ± .027	.050 ± .027	.063 ± .035	.075 ± .012	.090 ± .049	.090 ± .049	.090 ± .049	.269 ± .023	.269 ± .023	.085 ± .010	.047 ± .015				
P-wave duration	sec	.016 ± .002	.017 ± .001	.016 ± .003	.017 ± .001	.018 ± .001	.017 ± .001	.017 ± .001	.017 ± .001	.017 ± .001	.017 ± .001	.017 ± .001	.017 ± .001				
P-R interval	sec	.047 ± .006	.045 ± .004	.049 ± .007	.045 ± .003	.045 ± .002	.045 ± .004	.045 ± .004	.045 ± .004	.044 ± .002	.044 ± .002	.044 ± .002	.043 ± .002				
Q-R-S interval	sec	.016 ± .002	.016 ± .002	.016 ± .001	.016 ± .002	.017 ± .002	.015 ± .002	.015 ± .002	.015 ± .002	.016 ± .001	.016 ± .001	.016 ± .001	.016 ± .001				
Q-T interval	sec	.053 ± .005	.052 ± .005	.053 ± .005	.055 ± .006	.054 ± .007	.055 ± .006	.055 ± .006	.055 ± .006	.055 ± .004	.055 ± .004	.054 ± .005	.055 ± .004				
P-wave amplitude	mV	.24 ± .13	.25 ± .10	.23 ± .17	.36 ± .08	.34 ± .08	.38 ± .08	.38 ± .08	.38 ± .08	.24 ± .19	.24 ± .19	.37 ± .04	.07 ± .15				
T-wave amplitude	mV	.13 ± .05	.12 ± .06	.13 ± .03	.16 ± .05	.15 ± .05	.16 ± .05	.16 ± .05	.16 ± .05	.14 ± .04	.14 ± .04	.16 ± .04	.12 ± .03				
Treadmill run	min	12.6 ± 4.2	10.3 ± 4.0	14.8 ± 1.8	12.8 ± 4.1	12.6 ± 3.8	12.9 ± 4.8	12.9 ± 4.8	12.9 ± 4.8	10.9 ± 3.5	10.9 ± 3.5	11.7 ± 2.5	9.8 ± 5.0				

* Values indicate standard deviation.

* Student's 't' test - different from control at P = 0.01.

** Student's 't' test - different from control at P = 0.05.

*** Student's 't' test - different from control at P = 0.001.

Table B-17. Qualitative Observations on Rats Exposed to White Phosphorous/Felt Smoke

Observation	Number responding					
	Exposure period					
	6 Weeks			13 Weeks		
	Control	Low dose	High dose	Control	Low dose	High dose
Vasomotor reflex	12/12	12/12	6/6	12/12	12/12	7/7
Light reflex	12/12	12/12	6/6	12/12	12/12	7/7
Respiratory response to CO ₂	12/12	12/12	6/6	12/12	12/12	7/7
Sniffing response	9/12	12/12	6/6	11/12	12/12	7/7
Moist rales	0/12	0/12	0/6	0/12	0/12	3/12

Table B-18. Pulmonary Responses of Rats Exposed to White Phosphorus/Felt
Smoke for 13 Weeks

Condition	Sex	Number of animals	Response (mean and SE)		
			Estimated pulmonary resistance	Respiratory rate	Peak inspiratory flow
			cmH ₂ O/l/sec	resp/min	ml/sec
Control	Male	5	1.03 ± 0.06	179 ± 14.3	24.8 ± 0.92
High dose	Male	4	1.29 ± 0.18	171 ± 2.74	24.7 ± 0.70
Low dose	Male	5	1.75 ± 0.27	142 ± 5.07	24.1 ± 0.55
Control	Female	6	1.58 ± 0.88	120 ± 3.3	22.6 ± 0.90
High dose	Female	3	1.75 ± 0.27	145 ± 26.6	24.2 ± 0.59
Low dose	Female	6	1.33 ± 0.13	134 ± 5.8	23.3 ± 0.72

Table B-19. The Spontaneous Activity Responses of Rats Exposed to White Phosphorus/Felt Smoke

Condition	Sex	Number of animals	Response (mean and SE)		Gross activity ratios fine activity	
			Gross activity	Fine activity	from individual data	from mean
6-Week exposure						
Control	Female	6	457 \pm 143	1680 \pm 512	5.12 \pm 1.39	3.68
High dose	Female	3	502 \pm 21	1739 \pm 140	3.49 \pm 0.37	3.46
Low dose	Female	6	574 \pm 134	1874 \pm 353	6.32 \pm 3.40	3.20
Control	Male	6	278 \pm 122	1093 \pm 327	5.10 \pm 0.53	3.93
High dose	Male	3	336 \pm 65	723 \pm 319	1.97 \pm 0.37	2.15
Low dose	Male	6	760 \pm 109	2253 \pm 306	3.07 \pm 0.34	2.96
13-Week exposure						
Control	Female	6	608 \pm 133	160 \pm 300	2.82 \pm 0.46	2.65
High dose	Female	3	462 \pm 38	1548 \pm 149	3.42 \pm 0.53	3.35
Low dose	Female	6	575 \pm 177	1652 \pm 421	3.44 \pm 0.46	2.87
Control	Male	6	601 \pm 138	1287 \pm 176	2.40 \pm 0.29	2.14
High dose	Male	4	420 \pm 48	1368 \pm 308	2.86 \pm 0.54	2.91
Low dose	Male	6	450 \pm 123	1651 \pm 191	3.25 \pm 0.23	3.67

Table B-20. The Passive Avoidance Responses of Rats Exposed to White Phosphorus/Felt Smoke

Condition	Sex	Number of animals	Number of passive avoidance responses (mean and SE)	Total number of shocks (mean and SE)	Time in shock (mean and SE)
<u>6-Week exposure</u>					
Control	Female	6	3.3 ± 0.8	8.3 ± 2.8	0.86 ± 0.23
High dose	Female	3	4.7 ± 1.7	8.7 ± 5.6	0.84 ± 0.52
Low dose	Female	6	3.0 ± 1.0	7.0 ± 1.9	0.73 ± 0.19
Control	Male	6	2.7 ± 0.5	6.2 ± 1.9	0.72 ± 0.25
High dose	Male	3	5.3 ± 1.8	10.3 ± 3.3	1.24 ± 0.12
Low dose	Male	6	2.7 ± 0.5	6.0 ± 1.5	1.73 ± 0.32
<u>13-Week exposure</u>					
Control	Female	6	3.7 ± 0.8	9.3 ± 3.2	0.87 ± 0.35
High dose	Female	3	3.0 ± 0.6	10.7 ± 0.6	1.13 ± 0.15
Low dose	Female	6	7.7 ± 3.3	10.2 ± 2.7	1.21 ± 0.32
Control	Male	6	1.8 ± 0.3	7.0 ± 3.1	1.15 ± 0.64
High dose	Male	4	3.8 ± 1.2	25.5 ± 20.9	2.33 ± 1.89
Low dose	Male	6	2.3 ± 0.6	5.3 ± 2.4	0.55 ± 0.27

APPENDIX C

PATHOLOGY REPORT - SPONTANEOUS DEATHS

PATHOLOGY REPORT PROJECT SMOKE II, WHITE PHOSPHORUS/FELT INHALATION STUDY - SPONTANEOUS DEATHS "COLONY" RATS

I. INTRODUCTION.

Six and thirteen week studies designed to assess potential local and systemic toxic effects of inhalation exposure of the agent White Phosphorus/Felt were performed on Edgewood Area Colony Rats. Three dosage levels of the agent were tested. High (1000 mg/m³) dosage level studies began on 31 July 1978. Medium (500 mg/m³) dosage level studies began on 7 August 1978. Low (200 mg/m³) dosage level studies began on 11 September 1978. All rats were approximately six weeks of age at the beginning of the studies and were housed in Bldg E3266.

Of forty-three rats (19 male, 24 female) receiving the high (1000 mg/m³) dosage level exposure to White Phosphorus/Felt, twenty-nine (15 male, 14 female) died spontaneously during the studies while one control animal and none of the medium or low dose group animals died.

Following necropsy, tissues were imbedded in paraffin and subsequently processed for staining with hematoxylin and eosin. The following tissues were evaluated microscopically: nasal turbinate, larynx, trachea, lungs, heart, esophagus, stomach, small intestine, pancreas, large intestine, liver, adrenal, thyroid, thymus, kidney, bladder, ovary/teste, uterus, mammary gland, prostate, bone marrow, spleen, brain, eye and pituitary.

Histologic findings are tabulated in Tables 1-3. Since one or more tissues from various animals were lost at necropsy or during processing, one must calculate the incidence of lesions based upon the number of tissues examined rather than on the number of animals necropsied.

Two previous reports have been submitted regarding the histopathological findings in the colony rats that completed the six and thirteen week studies. This report deals only with the histopathological findings in those animals that died spontaneously before completing the studies.

II. RESULTS.

The microscopic observations are presented in the Histopathology Incidence Tables.

a. Table 1 tabulates incidence of lesions by organ observed in male and female rats dying spontaneously.

b. Table 2 tabulates incidence and severity of lesions by organ observed in male rats dying spontaneously from the high (1000 mg/m³) dosage level exposure group.

c. Table 3 tabulates incidence and severity of lesions by organ observed in female rats dying spontaneously from the high (1000 mg/m³) dosage level exposure group.

111. DISCUSSION.

Numerous sporadically occurring lesions were noted in the high (1000 mg/m³) dosage level rats that died prior to completion of the White Phosphorus/Felt smoke inhalation studies. Moderate to severe laryngitis was observed in all of nine male rats examined and in five out of six female rats examined. Moderate to severe tracheitis was observed in five out of seven male rats and in all of nine female rats examined. Laryngeal and tracheal lesions often included varying degrees of vessication (blistering) and ulceration of the mucosal surfaces. Death of many of these animals probably resulted from asphyxiation produced by mechanical blockage of the larynx/trachea from swelling or from laryngospasm resulting from irritation of the larynx by the smoke. Moderate to severe congestion (hyperemia) was observed in twenty-five out of twenty-nine lungs examined. Irritation produced by the inhaled smoke may be responsible for this finding. A minimal to mild multifocal to diffuse interstitial pneumonia was observed in sixteen out of twenty-nine lungs examined. Peribronchiolar lymphoid aggregates were noted in the lungs of eighteen of twenty-nine animals examined. The interstitial pneumonia and peribronchiolar lymphoid aggregates have been observed historically in colony rats held in this and adjacent animal research facilities. The death of one control rat is attributed to a generalized Phycomycosis (non-contagious fungal agent) involving the gastrointestinal tract, liver and brain.

IV. CONCLUSION.

A high mortality rate was noted in the high (1000 mg/m³) dosage level exposure group of colony rats being exposed to White Phosphorus/Felt smoke via inhalation exposure. The death of these animals appears to be agent and dose related. A moderate to severe laryngitis/tracheitis accompanied by varying degrees of vessication (blistering) and ulceration was observed in most of the animals. Death in these animals probably resulted from asphyxiation produced by mechanical blockage of the larynx/trachea from tissue swelling or from laryngospasm resulting from irritation of the larynx by the smoke. Moderate to severe pulmonary congestion was observed in many of the animals and is probably agent related.



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Project Smoke II
White Phosphorus/Felt
Inhalation Study - Spontaneous Deaths
"Colony" Rats

Key to Microscopic Findings

Table 1

Number of Animals: Represents total number of animals in each group necropsied.

Numbers following tissues represent the number of tissues from each group actually examined.

Numbers following lesions indicate the number of tissues examined showing the particular lesion.

Tables 2-3

- = tissue present

+ = tissue not available for microscopic evaluation

Numbers following organ: Number of specimens examined

Severity of Response

1 = Minimal

2 = Slight

3 = Moderate

4 = Severe

P = Present

STRAIN OF RAT: COLONY
EXPOSURE: VARIABLE
AGENT: WHITE PHOSPHORUS/FELT

[illegible]

TABLE 1 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II

		<u>CONTROL</u>						<u>HIGH DOSE</u>					
		M	F					M	F				
NUMBER OF ANIMALS													
HEART	1/15/14							1				15	14
Myocardial Fibrosis, Focal													
Myocarditis, Focal												2	3
ESOPHAGUS	0/13/13							0				13	13
STOMACH	1/15/14							1				15	14
Gastritis, Acute								1					
SMALL INTESTINE	1/13/13							1				13	13
Enteritis, Acute, Ulcerative								1					
PANCREAS	1/14/14							1				14	14
LARGE INTESTINE	1/14/13							1				14	13
Nematodiasis													
Enteritis, Acute								1					
LIVER	1/14/14							1				14	14
Hepatitis, Focal								1					
Infarct, Lobar													
ADRENAL	1/14/13							1				14	13

TABLE 1 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II

Appendix C

STRAIN OF RAT: COLONY
EXPOSURE: VARIABLE
AGENT: WHITE PHOSPHORUS/FELT

TABLE 1: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY UNIT:
SMOKE II

		CONTROL		HIGH DOSE	
		M	F	M	F
NUMBER OF ANIMALS					
MAMMARY GLAND	1/0/3	1		0	3
Adenoma				2	
Mastitis					
TESTES	0/15/0	0		15	0
PROSTATE	0/11/0	0		11	0
Prostatitis					
MARROW	1/9/8	1		9	8
Granulopoiesis, Accelerated					
SPLEEN	1/15/14	1		15	14
Hemosiderosis					4
Lymphoid Depletion		1			
BRAIN	1/15/14	1		15	14
Encephalitis, Pyogranulomatous					
Necrosis, Focal					
EYE	1/13/13	1		13	13
PITUITARY	1/7/4	1		7	4
Cvst					1

TABLE 2 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II

STRAIN OF RAT: COLONY
EXPOSURE: VARIABLE
DOSE LEVEL: HIGH (1000 MG/M³)
AGENT: WHITE PHOSPHORUS/FELT

MALE

	78-585	78-609	78-610	78-631	78-634	78-641	78-700	78-701	78-705	78-708	78-718	78-735	78-767	78-781	78-799
NASAL TURBINATE	12	-	+	+	+	-	-	-	-	-	-	-	-	-	+
Rhinitis, Focal															
LARYNX	9	+	-	-	-	-	+	+	-	+	-	-	+	-	+
Laryngitis		4	4	4	4	4			4	4	4	4		4	
Submucosal Gland Duct Ectasia												1			
TRACHEA	7	-	+	+	+	+	-	-	-	+	+	+	-	+	-
Tracheitis		3					4	4		3					4
Submucosal Gland Duct Ectasia															
LUNGS	15	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pneumonia, Interstitial		2		2	1	2	2	1	1	1	1				3
Pneumonia, Granulomatous															
Pneumonia, Purulent		2													
Congestion			3	4	3	3	3	3	3	3	3	3	3	3	3
Peribronchiolar Lymphoid		3				2	2	1	1	2	1	1	1	2	
Aggregates															
Bronchitis		2	2				2								

TABLE 2 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II

STRAIN OF RAT: COLONY
EXPOSURE: VARIABLE
DOSE LEVEL: HIGH (1000 MG/M³)
AGENT: WHITE PHOSPHORUS/FELT

MALE

HEART	15	78-585	-	78-609	-	78-610	-	78-631	-	78-634	-	78-641	-	78-700	-	78-701	-	78-705	-	78-708	-	78-718	-	78-735	-	78-767	-	78-781	-	78-799	-
Myocardial Fibrosis, Focal																		1 2													
Myocarditis, Focal																															
ESOPHAGUS	13		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	+	-	
STOMACH	15		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
SMALL INTESTINE	13		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	+	-	
PANCREAS	14		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	
LARGE INTESTINE	14		-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Nematodiasis																															
Enteritis, Acute																															
LIVER	14		-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Hepatitis, Focal																															
Infarct, Lobar																															
ADRENAL	14		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	

STRAIN OF RAT: COLONY
 EXPOSURE: VARIABLE
 DOSE LEVEL: HIGH (1000 MG/M³)
 AGENT: WHITE PHOSPHORUS/FELT
 TABLE 2 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
 SMOKE II

MALE

	78-585	78-609	78-610	78-631	78-634	78-641	78-700	78-701	78-705	78-708	78-718	78-735	78-767	78-781	78-799
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma															
Mastitis															
TESTES	15	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PROSTATE	11	+	+	-	-	-	-	-	-	-	-	-	-	+	-
Prostatitis															
MARROW	9	+	-	-	+	+	-	+	-	+	-	-	-	-	-
Granulopoiesis, Accelerated															
SPLEEN	15	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hemosiderosis															
BRAIN	15	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Encephalitis, Pyogranulomatous															
Necrosis, Focal															
EYE	13	-	-	-	-	-	-	+	-	+	+	-	-	-	-
PITUITARY	7	+	+	+	+	+	+	-	-	-	+	-	-	-	-
Adenoma															

TABLE 2 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE 11

STRAIN OF RAT: COLONY
EXPOSURE: VARIABLE
DOSE LEVEL: HIGH (1000 MG/M³)
AGENT: WHITE PHOSPHORUS/FELT

MALE

	78-585	78-609	78-610	78-631	78-634	78-641	78-700	78-701	78-705	78-708	78-718	78-735	78-767	78-781	78-799
THYROID	-	-	-	+	+	-	-	-	-	-	+	+	-	+	-
Degeneration	3	2	1			3	3	2					1		4
THYMUS	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-
Hemorrhage, Focal															
KIDNEY	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hydronephrosis															
Nephritis, Interstitial										3					1
Glomerulonephritis															
Tubular Mineralization, Focal															
Tubular Dilatation, Focal	3			2	2					3					
Proteinuria															
BLADDER	-	-	+	-	-	+	+	+	+	-	+	+	+	+	+
Perivasculitis															
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Metritis															

TABLE 3 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II

STRAIN OF RAT: COLONY
EXPOSURE: VARIABLE
DOSE LEVEL: HIGH (1000 MG/M³)
AGENT: WHITE PHOSPHORUS/FELT

FEMALE

	78-583	78-614A	78-614B	78-620	78-621	78-622	78-640	78-642	78-643	78-665	78-703	78-709	78-724	78-797
NASAL TURBINATE	11	-	-	-	-	+	-	-	-	+	-	-	+	-
Rhinitis, Focal											3	2		
LARYNX	6	+	-	-	+	+	-	-	+	+	-	-	+	+
Laryngitis			4	4			4	4			3			
Submucosal Gland Duct Ectasia														
TRACHEA	9	-	+	+	-	-	+	-	-	-	+	+	-	-
Tracheitis		3	4		3	4		4	3	4			4	4
Submucosal Gland Duct Ectasia										2				
LUNGS	14	-	-	-	-	-	-	-	-	-	-	-	-	-
Pneumonia, Interstitial		2	2	2			1	1	2	1	1			2
Pneumonia, Granulomatous														
Pneumonia, Purulent					3	1								
Congestion	1	1	3	2	4	3	3	3	4	4	3	3	3	3
Peribronchiolar Lymphoid		1	1	1	1	1	1	2	2	2			1	
Aggregates														
Bronchitis														

STRAIN OF RAT: COLONY
EXPOSURE: VARIABLE
DOSE LEVEL: HIGH (1000 MG/M³)
AGENT: WHITE PHOSPHORUS/FELT

[illegible]

STRAIN OF RAT: COLONY
 EXPOSURE: VARIABLE
 DOSE LEVEL: HIGH (1000 MG/M³)
 AGENT: WHITE PHOSPHORUS/FELT

TABLE 3 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
 SMOKE II

FEMALE

	78-583	78-614A	78-614B	78-620	78-621	78-622	78-640	78-642	78-643	78-665	78-703	78-709	78-724	78-797
THYROID														
Degeneration	2	1	2	3	2		+	-	-	-	-	-	-	-
THYMUS														
Hemorrhage, Focal	-	+	+	+	+		+	-	-	-	-	+	+	-
KIDNEY														
Hydronephrosis	-	-	-	-	-		-	-	-	-	-	-	-	-
Nephritis, Interstitial			1					2						
Glomerulonephritis					2									
Tubular Mineralization, Focal	1	1	1				2		1				2	
Tubular Dilatation, Focal														
Proteinuria		1	2	1	3									
BLADDER														
Perivasculitis	-	-	-	-	-		-	-	-	-	-	-	-	-
OVARY														
	-	-	-	-	-		-	-	-	-	-	-	-	-
UTERUS														
	-	-	+	-	-		-	+	-	-	-	-	-	+
Metritis														

STRAIN OF RAT: COLONY
 EXPOSURE: VARIABLE
 DOSE LEVEL: HIGH (1000 MG/M³)
 AGENT: WHITE PHOSPHORUS/FEET
 TABLE 3 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
 SMOKE II

FEMALE

	78-583	78-614A	78-614B	78-620	78-621	78-622	78-640	78-642	78-643	78-665	78-703	78-709	78-724	78-797
MAMMARY GLAND	3													
Adenoma														
Mastitis														
TESTES	0													
PROSTATE	0													
Prostatitis														
MARROW	8													
Granulopoiesis, Accelerated														
SPLEEN	14													
Hemosiderosis	1													
BRAIN	14													
Encephalitis, Pyogranulomatous														
Necrosis, Focal														
EYE	13													
PITUITARY	4													
Cyst														

APPENDIX D
PATHOLOGY REPORT - 6-WEEK EXPOSURE

Project Smoke II
Inhalation Study Six Weeks
"Colony" Rats

1. Introduction.

The present study was designed to assess potential local and toxic effects following inhalation exposure to White Phosphorus/Felt for a period of fifteen minutes per day, five days a week, for six weeks.

A group of six female rats were exposed by the inhalation route to White Phosphorus/Felt at a high dose level (1000 mg/m^3) and two groups of twelve rats, equally divided as to sex, received intermediate (500 mg/m^3) and low (200 mg/m^3) dosage levels for the prescribed period of time followed by euthanasia. A fourth group of eighteen rats, equally divided as to sex, that were exposed to air only and maintained under similar conditions, served as controls.

At termination and necropsy, tissues were imbedded in paraffin and subsequently processed for staining with hematoxylin and eosin. The following tissues were evaluated microscopically: nasal turbinate, larynx, trachea, lungs, heart, esophagus, stomach, small intestine, pancreas, large intestine, liver, adrenal, thyroid, thymus, kidney, bladder, ovary/teste, uterus, mammary gland, prostate, bone marrow, spleen, brain, eye and pituitary.

2. Results.

The microscopic observations are presented in the Histopathology Incidence Tables.

a. Tables 1-4 tabulate incidence of lesions (by organ) observed in the four groups of male and female colony rats.

b. Tables 5-8 tabulate incidence and severity of lesions (by organ) observed in male and female control rats.

c. Tables 9-12 tabulate incidence of lesions (by organ) observed in each female rat receiving the high dose level exposure to White Phosphorus/Felt.

d. Tables 13-16 tabulate incidence of lesions (by organ) observed in each male and female rat receiving the intermediate dose level exposure to White Phosphorus/Felt.

3. Discussion.

A number of spontaneous lesions were noted in the liver, kidney, thyroid, and pituitary; the lesions occurring with equal severity and frequency in control and White Phosphorus/Felt exposed rats. While none of the control animals displayed laryngitis or tracheitis, all of the laryngeal and tracheal specimens examined from the rats receiving the high dosage level of White Phosphorus/Felt displayed a moderate to severe laryngitis/tracheitis. Fifty percent of the rats receiving intermediate dose levels of White Phosphorus/Felt displayed a minimal to mild tracheitis while one out of three rats had a mild laryngitis. Only one rat receiving the low dose level of White Phosphorus/Felt displayed tracheitis. Four out of six female rats receiving the high dose level of White Phosphorus/Felt displayed minimal to severe interstitial pneumonia while one control rat of each sex displayed a minimal interstitial pneumonia.

4. Conclusion.

The agent, White Phosphorus/Felt, at the dosage levels tested and in the manner tested show a dose related laryngitis and tracheitis. It is suggestive

that high dosage levels of White Phosphorus/Felt may produce interstitial pneumonia in some animals.



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Project Smoke II
White Phosphorus Felt
Inhalation Study Six Weeks
"Colony" Rats

Key to Microscopic Findings

Tables 1-4

Number of Animals: Represents total number of animals in each group utilized in the study.

Numbers following tissues represent the number of tissues from each group actually examined.

Numbers following lesion indicate the number of tissues examined showing the particular lesion.

Tables 5-16

- = tissue present

* = tissue not available for microscopic evaluation

Severity of Response

1 = minimal

2 = slight

3 = moderate

4 = severe

P = present

TABLE 1: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II, 6 WEEKS EXPOSURE

STRAIN OF RAT: COLONY
WEEKS EXPOSURE: 6
DAYS POST EXPOSURE: 1
AGENT: WHITE PHOSPHORUS FELT

	CONTROL		HIGH		INTERMEDIATE		LOW	
	M	F	M	F	M	F	M	F
NUMBER OF ANIMALS	9	9		6	6	6	6	6
NASAL TURBINATE	7	8		5	4	3		
Rhinitis, Focal								
LARYNX	7	4		2	0	3	0	2
Laryngitis				2	1	1		1
Submucosal Gland Duct Ectasia	3	2		1				
TRACHEA	3	7		4	6	4	6	3
Tracheitis				4	3	2	1	1
Submucosal Gland Duct Ectasia		2						
LUNGS	9	9		6	6	6	6	6
Pneumonia, Interstitial	1	1		4	2	1	1	
Pneumonia, Granulomatous								
Pneumonia, Purulent				1	2		2	
Congestion				1				
Peribronchiolar Lymphoid	6	4		3	5	5	3	5
Aggregates								
Bronchitis				3				

TABLE 2: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II, 6 WEEKS EXPOSURE

STRAIN OF RAT: COLONY
WEEKS EXPOSURE: 6
DAYS POST EXPOSURE: 7
AGENT: WHITE PHOSPHORUS FELT

NUMBER OF ANIMALS	CONTROL		HIGH		INTERMEDIATE		LOW	
	M	F	M	F	M	F	M	F
HEART	9	9			6	6	6	6
Myocardial Fibrosis, Focal		7			1			
Myocarditis, Focal	3						1	
ESOPHAGUS	9	8	5		6	6	6	6
STOMACH	9	9	6		6	5	5	6
SMALL INTESTINE	9	9	5		6	6	6	4
PANCREAS	9	9	6		5	5	6	6
LARGE INTESTINE	9	9	6		6	4	6	6
Hematomiasis	1				1			
Enteritis, Acute								
LIVER	9	9	6		6	6	6	6
Hepatitis, Focal		3						
Infarct, Lobar								
ADRENAL	9	9	6		5	5	6	6

TABLE 3: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II, 6 WEEKS EXPOSURE.

STRAIN OF RAT: COLONY
WEEKS EXPOSURE: 6
DAYS POST EXPOSURE: 1
AGENT: WHITE PHOSPHORUS FELT

	CONTROL		HIGH		INTERMEDIATE		LOW	
	M	F	M	F	M	F	M	F
NUMBER OF ANIMALS	9	9	0	6	6	6	6	6
THYROID	8	7		4	5	3	5	6
Degeneration	7	4		2	3	2	2	3
THYMUS	9	7		4	5	5	5	5
Hemorrhage, Focal								
KIDNEY	9	9		6	6	6	6	6
Hydronephrosis	1	1		1				
Nephritis, Interstitial		1						
Glomerulonephritis								
Tubular Mineralization, Focal		6		5		5	1	2
Tubular Dilatation, Focal		1						
Proteinuria	1	1			1			1
BLADDER	7	7		3				
Perivasculitis								
OVARY	0	9		6		5	0	6
UTERUS								
Metritis		8		6		4	0	4
				1				

TABLE 4: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SNOKE II, 6 WEEKS EXPOSURE.

STRAIN OF RAT: COLONY
WEEKS EXPOSURE: 6
DAYS POST EXPOSURE: 1
AGENT: WHITE PHOSPHORUS FELT

NUMBER OF ANIMALS	CONTROL		HIGH		INTERMEDIATE		LOW	
	M	F	M	F	M	F	M	F
MAMMARY GLAND	0	2		3	0	4	0	1
Adenoma								
Mastitis								
TESTES	9	0		0	6	0	6	0
PROSTATE	9	0		0	4	0	6	0
Prostatitis								
MARROW	6	8		5	4	6	6	6
Granulopoiesis, Accelerated	1			1		2		
SPLEEN	9	8		6	6	6	6	6
Hemosiderosis		4		2		3		1
BRAIN	9	9		6	5	6	6	6
Encephalitis, Pyogranulomatous								
Necrosis, Focal								
EYE	7	9		5	5	5	5	6
PITUITARY	5	7		6	4	4	6	6
Adenoma		1						

TABLE 5: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II, 6 WEEKS EXPOSURE

STRAIN OF RAT: COLONY
WEEKS EXPOSURE: 6
DAYS POST EXPOSURE: 1
DOSE LEVEL: Control
NECROPSY NO: 78-800/801/731/730/745/746
AGENT: WHITE PHOSPHORUS FELT

FEMALE

MALE

	A	B	C	D	E	F	G	H	I	J	A	B	C	D	E	F	G	H	I	J
NASAL TURBINATE	-	*	-	-	-	-	*	-	-	-	-	-	-	-	-	-	*	-	-	-
Rhinitis, Focal																				
LARYNX	*	-	*	-	-	-	-	-	-	-	*	-	*	-	*	-	-	-	*	-
Laryngitis																				
Submucosal Gland Duct Ectasia							1	3	1				3			2				
TRACHEA	-	-	-	*	*	*	*	*	*	*	-	-	*	*	*	-	-	-	-	-
Tracheitis																				
Submucosal Gland Duct Ectasia															1					1
LUNGS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pneumonia, Interstitial						2							2							
Pneumonia, Granulomatous																				
Pneumonia, Purulent																				
Congestion																				
Peribronchiolar Lymphoid				1	1	1	1	1	1				1		1				1	
Aggregates																				
Bronchitis																				

TABLE 6: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II, 6 WEEKS EXPOSURE

STRAIN OF RAT: COLONY
WEEKS EXPOSURE: 6
DAYS POST EXPOSURE: 1
DOSE LEVEL: Control
NECROPSY NO: 78-800/801/731/730/745/746
AGENT: WHITE PHOSPHORUS FELT

FEMALE

MALE

	A	B	C	D	E	F	G	H	I	J	A	B	C	D	E	F	G	H	I	J
HEART	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Myocardial Fibrosis, Focal													2							
Myocarditis, Focal	2						1	1												
ESOPHAGUS	-	-	-	-	-	-	-	-	-	-	-	*	-	*	-	-	-	-	-	-
STOMACH	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
SMALL INTESTINE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PANCREAS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
LARGE INTESTINE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Nematodiasis																				
Enteritis, Acute																				
LIVER	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hepatitis, Focal											1	1	1							
Infarct, Lobar																				
ADRENAL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

TABLE 7: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II, 6 WEEKS EXPOSURE

STRAIN OF RAT: COLONY
WEEKS EXPOSURE: 6
DAYS POST EXPOSURE: 1
DOSE LEVEL: Control
NECROPSY NO: 78-800/801/731/730/745/746
AGENT: WHITE PHOSPHORUS FELT

FEMALE

MALE

	A	B	C	D	E	F	G	H	I	J	A	B	C	D	E	F	G	H	I	J
THYROID	*	-	-	-	-	-	-	-	-	-	-	*	-	-	-	*	-	-	-	-
Degeneration	4	3	3	1	2	2	2	2	2	2				4	2		4		3	
THYMUS	-	-	-	-	-	-	-	-	-	-	-	*	*	-	-	-	-	-	-	-
Hemorrhage, Focal																				
KIDNEY	-	-	-	-	-	-	-	-	-	-	-	-	2							
Hydronephrosis							3												2	
Nephritis, Interstitial																				
Glomerulonephritis												2								
Tubular Mineralization, Focal															1					
Tubular Dilatation, Focal							1					1								
Proteinuria																				
BLADDER	*	-	-	-	-	-	*	-	-	-	-	-	-	-	-	-	*	*	-	-
Perivasculitis																				
OVARY																				
UTERUS												*	*	-	-	-	-	-	-	-
Metritis																				

3

TABLE 8: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II, 6 WEEKS EXPOSURE

STRAIN OF RAT: COLONY
WEEKS EXPOSURE: 6
DAYS POST EXPOSURE: 1
DOSE LEVEL: Control
NECROPSY NO: 78-800/801/731/730/745/746
AGENT: WHITE PHOSPHORUS FELT

FEMALE

MALE

	A	B	C	D	E	F	G	H	I	J	A	B	C	D	E	F	G	H	I	J
MAMMARY GLAND											*	*	*	*	*	*	*	*	*	*
Adenoma																				
Mastitis																				
TESTES	-	-	-	-	-	-	-	-	-	-										
PROSTATE	-	-	-	-	-	-	-	-	-	-										
Prostatitis																				
MARROW	*	-	-	-	-	-	*	*	*	*	-	*	*	*	*	*	*	*	*	*
Granulopoiesis, Accelerated			2																	
SPLEEN	-	-	-	-	-	-	-	-	-	-	*	*	*	*	*	*	*	*	*	*
Hemosiderosis											2	2	1							2
BRAIN	-	-	-	-	-	-	-	-	-	-										
Encephalitis, Pyogranulomatous																				
Necrosis, Focal	*	-	-	-	*	*	*	*	*	*	-	*	*	*	*	*	*	*	*	*
EYE	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
PITUITARY																				
Adenoma																				P

TABLE 9: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II, 6 WEEKS EXPOSURE

STRAIN OF RAT: COLONY
WEEKS EXPOSURE: 6
DAYS POST EXPOSURE: 1
DOSE LEVEL: High
NECROPSY NO: 78-728/729
AGENT: WHITE PHOSPHORUS FELT

Appendix D

MALE

FEMALE

	A	B	C	D	E	F	G	H	I	J		A	B	C	D	E	F	G	H	I	J
NASAL TURBINATE																					
Rhinitis, Focal																					
LARYNX																					
Laryngitis																					
Submucosal Gland Duct Ectasia																					
TRACHEA																					
Tracheitis																					
Submucosal Gland Duct Ectasia																					
LUNGS																					
Pneumonia, Interstitial																					
Pneumonia, Granulomatous																					
Pneumonia, Purulent																					
Congestion																					
Peribronchiolar Lymphoid																					
Aggregates																					
Bronchitis																					

STRAIN OF RAT: COLONY
 WEEKS EXPOSURE: 6
 DAYS POST EXPOSURE: 7
 DOSE LEVEL: High
 NECROPSY NO: 78-728/729
 AGENT: WHITE PHOSPHORUS FELT

MALE FEMALE

	A	B	C	D	E	F	G	H	I	J	A	B	C	D	E	F	G	H	I	J
HEART																				
Myocardial Fibrosis, Focal																				
Myocarditis, Focal																				
ESOPHAGUS																				
STOMACH																				
SMALL INTESTINE																				
PANCREAS																				
LARGE INTESTINE																				
Nematodiasis																				
Enteritis, Acute																				
LIVER																				
Hepatitis, Focal																				
Infarct, Lobar																				
ADRENAL																				

TABLE 1: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II 6 WEEKS EXPOSURE

STRAIN OF RAT: COLONY
WEEKS EXPOSURE: 6
DAYS POST EXPOSURE: 7
DOSE LEVEL: High
NECROPSY NO: 78-728/729
AGENT: WHITE PHOSPHORUS FELT

FEMALE

MALE

	A	B	C	D	E	F	G	H	I	J		A	B	C	D	E	F	G	H	I	J
THYROID																					
Degeneration																					
THYMUS																					
Hemorrhage, Focal																					
KIDNEY																					
Hydronephrosis																					
Nephritis, Interstitial																					
Glomerulonephritis																					
Tubular Mineralization, Focal																					
Tubular Dilatation, Focal																					
Proteinuria																					
BLADDER																					
Perivascularitis																					
OVARY																					
UTERUS																					
Metritis																					

TABLE 12: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II, 6 WEEKS EXPOSURE

STRAIN OF RAT: COLONY
WEEKS EXPOSURE: 6
DAYS POST EXPOSURE: 1
DOSE LEVEL: High
NECROPSY NO: 78-728/729
AGENT: WHITE PHOSPHORUS FELT

MALE FEMALE

	A	B	C	D	E	F	G	H	I	J	A	B	C	D	E	F	G	H	I	J
MAMMARY GLAND											*	-	*	*	-					
Adenoma																				
Mastitis																				
TESTES											*	*	*	*	*	*	*	*	*	*
PROSTATE											*	*	*	*	*	*	*	*	*	*
Prostatitis																				
MARROW											-	-	*	-	-	-	-	-	-	-
Granulopoiesis, Accelerated																				2
SPLEEN											-	-	-	-	-	-	-	-	-	-
Hemosiderosis															1	1				
BRAIN											-	-	-	-	-	-	-	-	-	-
Encephalitis, Pyogranulomatous																				
Necrosis, Focal											-	-	-	-	*	*	*	*	*	*
EYE																				
PITUITARY											-	-	-	-	-	-	-	-	-	-
Adenoma																				

TABLE 13: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II, 6 WEEKS EXPOSURE

STRAIN OF RAT: COLONY
WEEKS EXPOSURE: 6
DAYS POST EXPOSURE: 1
DOSE LEVEL: Intermediate
NECROPSY NO: 78-747748
AGENT: WHITE PHOSPHORUS FELT

Appendix D

MALE FEMALE

	A	B	C	D	E	F	G	H	I	J	A	B	C	D	E	F	G	H	I	J
NASAL TURBINATE	-	*	-	*	-	-					-	*	-	*	-	*				
Rhinitis, Focal																				
LARYNX	*	*	*	*	*	*					-	*	-	*	-	*				
Laryngitis														2						
Submucosal Gland Duct Ectasia														3						
TRACHEA	-	-	-	-	-	-					-	*	-	*	-	-				
Tracheitis	2	1	2								2					1				
Submucosal Gland Duct Ectasia																				
LUNGS	-	-	-	-	-	-					-	-	-	-	-	-				
Pneumonia, Interstitial					1	3					4									
Pneumonia, Granulomatous																				
Pneumonia, Purulent																				
Congestion			3	2																
Peribronchiolar Lymphoid	1	1	1	2	1						1	1	1	1	1	1				
Aggregates																				
Bronchitis																				

STRAIN OF RAT: COLONY
 WEEKS EXPOSURE: 6
 DAYS POST EXPOSURE: 1
 DOSE LEVEL: Intermediate
 NECROPSY NO: 78-747/742
 AGENT: WHITE PHOSPHORUS FELT

TABLE 1: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
 SMOKE II, 6 WEEKS EXPOSURE

MALE

FEMALE

	A	B	C	D	E	F	G	H	I	J	A	B	C	D	E	F	G	H	I	J
HEART	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Myocardial Fibrosis, Focal						2														
Myocarditis, Focal																				
ESOPHAGUS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
STOMACH	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
SMALL INTESTINE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PANCREAS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
LARGE INTESTINE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Nematodiasis																				
Enteritis, Acute																				
LIVER	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hepatitis, Focal																				
Infarct, Lobar																				
ADRENAL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

STRAIN OF RAT: COLONY
 WEEKS EXPOSURE: 6
 DAYS POST EXPOSURE: 1
 DOSE LEVEL: Intermediate
 NECROPSY NO: 78-747/748
 AGENT: WHITE PHOSPHORUS FELT

TABLE 15: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
 SMOKE II, 6 WEEKS EXPOSURE

	MALE										FEMALE									
	A	B	C	D	E	F	G	H	I	J	A	B	C	D	E	F	G	H	I	J
THYROID	-	-	*	-	-	-	-	-	-	-	-	*	*	*	-	-	-	-	-	-
Degeneration				4	3	2									4	3				
THYMUS	*	-	-	-	-	-	-	-	-	-	-	-	-	-	-	*				
Hemorrhage, Focal				1																
KIDNEY	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hydronephrosis																				
Nephritis, Interstitial																				
Glomerulonephritis											2	1	2	1	1					
Tubular Mineralization, Focal																				
Tubular Dilatation, Focal																				
Proteinuria						1														
BLADDER	*	*	*	*	*	-	-	-	-	-	-	*	*	*	*	*	*	*	*	*
Perivasculitis																				
OVARY											-	*	*	*	*	*	*	*	*	*
UTERUS											-	*	*	*	*	*	*	*	*	*
Metritis																				

TABLE 16: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SHOKE II, 6 WEEKS EXPOSURE

STRAIN OF RAT: COLONY
WEEKS EXPOSURE: 6
DAYS POST EXPOSURE: 1
DOSE LEVEL: Intermediate
NECROPSY NO: 78-747/743
AGENT: WHITE PHOSPHORUS FELT

MALE FEMALE

	A	B	C	D	E	F	G	H	I	J	A	B	C	D	E	F	G	H	I	J
MAMMARY GLAND											*	-	-	*	*	*				
Adenoma																				
Mastitis																				
TESTES	-	-	-	-	-	-														
PROSTATE	-	*	-	-	-	*														
Prostatitis																				
MARROW	-	*	-	-	-	*					-	-	-	-	-	-	-	-	-	-
Granulopoiesis, Accelerated												3				2				
SPLEEN	-	-	-	-	-	-					-	-	-	-	-	-	-	-	-	-
Hemosiderosis											1	1					1			
BRAIN	-	*	-	-	-	-					-	-	-	-	-	-	-	-	-	-
Encephalitis, Pyogranulomatous																				
Necrosis, Focal	-	-	*	-	-	-					-	-	-	-	-	-	*			
EYE	-	-	*	*	*	*					-	-	*	*	*	*	*	*	*	*
PITUITARY																				
Adenoma																				

STRAIN OF RAT: COLONY
 WEEKS EXPOSURE: 6
 DAYS POST EXPOSURE: 1
 DOSE LEVEL: LOW
 NECROPSY NO: 78-796/798
 AGENT: WHITE PHOSPHORUS FELT

TABLE 17: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
 SMOKE II, 6 WEEKS EXPOSURE

MALE

FEMALE

	A	B	C	D	E	F	G	H	I	J	A	B	C	D	E	F	G	H	I	J
NASAL TURBINATE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Rhinitis, Focal																				
LARYNX	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Laryngitis																				
Submucosal Gland Duct Ectasia																				
TRACHEA	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Tracheitis																				
Submucosal Gland Duct Ectasia	2	2	2	2	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1
LUNGS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pneumonia, Interstitial																				
Pneumonia, Granulomatous																				
Pneumonia, Purulent																				
Congestion																				
Peribronchiolar Lymphoid	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Aggregates																				
Bronchitis																				

TABLE 18: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE 11, 6 WEEKS EXPOSURE

STRAIN OF RAT: COLONY
WEEKS EXPOSURE: 6
DAYS POST EXPOSURE: 1
DOSE LEVEL: LOW
NECROPSY NO: 78-796/798
AGENT: WHITE PHOSPHORUS-FELT

MALE FEMALE

	A	B	C	D	E	F	G	H	I	J	A	B	C	D	E	F	G	H	I	J
HEART	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Myocardial Fibrosis, Focal																				
Myocarditis, Focal																				
ESOPHAGUS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
STOMACH	-	-	-	*	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
SMALL INTESTINE	-	-	-	-	-	-	-	-	-	-	-	-	-	*	-	-	-	-	-	-
PANCREAS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
LARGE INTESTINE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Nematodiasis																				
Enteritis, Acute																				
LIVER	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hepatitis, Focal																				
Infarct, Lobar																				
ADRENAL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

TABLE 19: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II, 6 WEEKS EXPOSURE

STRAIN OF RAT: COLONY
WEEKS EXPOSURE: 6
DAYS POST EXPOSURE: 1
DOSE LEVEL: Low
NECROPSY NO: 78-796/798
AGENT: WHITE PHOSPHORUS FELT

	MALE										FEMALE									
	A	B	C	D	E	F	G	H	I	J	A	B	C	D	E	F	G	H	I	J
THYROID	-	-	*	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Degeneration	3			2							3	1		2						
THYMUS	*	-	-	-	-	-	-	-	-	-	-	-	-	*						
Hemorrhage, Focal																				
KIDNEY	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hydronephrosis																				
Nephritis, Interstitial																				
Glomerulonephritis	1												2			1				
Tubular Mineralization, Focal																				
Tubular Dilatation, Focal											1									
Proteinuria																				
BLADDER	-	*	*	*	*	*	*	*	*	*	-	*	*	*	*	*	*	*	*	*
Perivasculitis																				
OVARY																				
UTERUS																				
Metritis																				

TABLE 20: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SROKE II, 6 WEEKS EXPOSURE

STRAIN OF RAT: COLONY
WEEKS EXPOSURE: 6
DAYS POST EXPOSURE: 1
DOSE LEVEL: Low
NECROPSY NO: 78-796/798
AGENT: WHITE PHOSPHORUS FELT

MALE

FEMALE

	A	B	C	D	E	F	G	H	I	J	A	B	C	D	E	F	G	H	I	J
MAMMARY GLAND																				
Adenoma																				
Mastitis																				
TESTES																				
PROSTATE																				
Prostatitis																				
MARROW																				
Granulopoesis, Accelerated																				
SPLEEN																				
Hemosiderosis																				
BRAIN																				
Encephalitis, Pyogranulomatous																				
Necrosis, Focal																				
EYE																				
PITUITARY																				
Adenoma																				

APPENDIX E

PATHOLOGY REPORT - 13-WEEK EXPOSURE

PATHOLOGY REPORT PROJECT SMOKE II, WHITE PHOSPHORUS/FELT INHALATION STUDY - THIRTEEN WEEKS "COLONY" RATS

I. INTRODUCTION.

The study was designed to assess potential local and systemic toxic effects on Edgewood Area Colony rats following inhalation exposure in a chamber to White Phosphorus/Felt for a period of fifteen minutes per day, five days a week, for thirteen weeks. Three separate dosage levels were studied with each dosage level beginning on a different date and having a separate set of control animals receiving sham treatment and housing under similar conditions. All animals were approximately six weeks of age at the beginning of each study. The exposures and animal holding were performed in Bldg E3266.

Exposure of the high dose (1000 mg/m^3) group began on 31 July and ended on 31 October 1978. The exposed group consisted of eight animals, four of each sex. A separate group of three male and three female controls were utilized. Exposure of the medium dose (500 mg/m^3) group began on 7 August 1978 and ended on 7 November of that year. Twelve rats, six of each sex, were exposed to the agent. Three male and three female control rats were utilized in this study. Exposure of the low dose (200 mg/m^3) began on 11 September 1978 and ended on 12 December of the same year. A group of twelve animals, six of each sex, were exposed to the agent. Three male and three female controls were utilized in the study.

In addition to the above animals, a total of four rats, two of each sex, that had been exposed with the high dose group and utilized in physiology studies for eight days were necropsied. No controls were submitted with this group of animals. These animals were included separately in Tables 17-20, but are not considered part of the study in interpreting pathology findings.

Following necropsy, tissues were imbedded in paraffin and subsequently processed for staining with hematoxylin and eosin. The following tissues were evaluated microscopically: nasal turbinate, larynx, trachea, lungs, heart, esophagus, stomach, small intestine, pancreas, large intestine, liver, adrenal, thyroid, thymus, kidney, bladder, ovary/teste, uterus, mammary gland, prostate, bone marrow, spleen, brain, eye and pituitary.

Histologic findings are tabulated in Tables 1-20. Since one or more tissues from various animals were lost at necropsy or during processing, one must calculate the incidence of lesions based upon the number of tissues examined rather than on the number of animals necropsied.

II. RESULTS.

The microscopic observations are presented in the Histopathology Incidence Tables.

a. Tables 1-4 tabulate incidence of lesions (by organ) observed in the six groups of male and female colony rats utilized in the three studies.

b. Tables 5-8 tabulate incidence and severity of lesions (by organ) observed in male and female control rats.

c. Tables 9-12 tabulate incidence of lesions (by organ) observed in each male and female rat receiving the high dose (1000 mg/m³) level exposure to White Phosphorus/Felt.

d. Tables 13-16 tabulate incidence of lesions (by organ) observed in each male and female rat receiving the medium dose (500 mg/m³) level exposure.


e. Table 17-20 tabulate incidence of lesions (by organ) observed in each male and female rat receiving the low dose (200 mg/m³) level exposure.

III. DISCUSSION.

A number of spontaneous lesions were noted in the liver, kidney, thyroid, spleen, heart, uterus, bladder, mammary glands and large intestine. The lesions occurred either sporadically or with equal frequency and severity in both control and White Phosphorus/Felt exposed rats. While none of the control rats displayed laryngitis or tracheitis, all of the male rats receiving the high dosage level of White Phosphorus/Felt exhibited a moderate laryngitis. Of the female rats receiving the same dosage level (1000 mg/m³) of White Phosphorus/Felt, one of two larynges examined displayed a moderate laryngitis while two out of three tracheae displayed mild to moderate tracheitis. Three out of six female rats receiving the medium dosage level of White Phosphorus/Felt displayed a moderate tracheitis while three out of five male rats receiving the same level exposure displayed slight to moderate tracheitis. None of the low dosage level animals displayed laryngitis or tracheitis.

IV. CONCLUSION.

Though the small number of tissues examined prevents a definitive conclusion, it appears that the agent, White Phosphorus/Felt produces a dose related laryngitis and tracheitis when rats are exposed in the manner tested.


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Project Smoke II
White Phosphorus/Felt
Inhalation Study - Thirteen Weeks
"Colony" Rats

Key to Microscopic Findings

Tables 1-4

Number of Animals: Represents total number of animals in each group utilized in the study.

Numbers following tissues represent the number of tissues from each group actually examined.

Numbers following lesions indicate the number of tissues examined showing the particular lesion.

Tables 5-20

- = tissue present

+ = tissue not available for microscopic evaluation

Numbers Following Organs: First number is number of tissues from males examined, second number is number of tissues from females.

Severity of Response

1 = Minimal

2 = Slight

3 = Moderate

4 = Severe

P = Present

TABLE 1 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II

STRAIN OF RAT: Colony
EXPOSURE: 13 wks
AGENT: White Phosphorus/Feit

	HIGH DOSE				MEDIUM DOSE				LOW DOSE			
	CONTROL		EXPOSED		CONTROL		EXPOSED		CONTROL		EXPOSED	
	M	F	M	F	M	F	M	F	M	F	M	F
NUMBER OF ANIMALS	3	3	4	4	3	3	6	6	3	3	6	6
NASAL TURBINATE	3	2	3	3	3	2	4	6	2	3	6	6
Rhinitis, Focal												
LARYNX	3	2	2	2	0	1	0	0	2	0	1	4
Laryngitis	1	1	2	1							4	
Submucosal Gland Duct Ectasia							5	6	3	3	5	4
TRACHEA	1	2	0	3	3	3	3	3				
Tracheitis			2						1		1	
Submucosal Gland Duct Ectasia												
LUNGS	3	3	4	4	3	3	6	6	3	3	6	6
Pneumonia, Interstitial	1		1	1	1	1	1	1				
Pneumonia, Granulomatous												
Pneumonia, Purulent												
Congestion												
Peribronchioal Lymphoid	3	1	2		3	2	5	6	3	2	4	5
Aggregates												
Bronchitis												

TABLE 2 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II

STRAIN OF RAT: Colony
EXPOSURE: 13 wks
AGENT: White Phosphorus/Felt

	HIGH DOSE						MEDIUM DOSE						LOW DOSE					
	CONTROL			EXPOSED			CONTROL			EXPOSED			CONTROL			EXPOSED		
	M	F		M	F		M	F		M	F		M	F		M	F	
NUMBER OF ANIMALS	3	3		4	4		3	3		6	6		3	3		6	6	
HEART	3	3		4	4		3	3		6	6		3	3		6	6	
Myocardial Fibrosis, Focal																		
Myocarditis, Focal				1						3			2					
ESOPHAGUS	3	3		3	3		3	3		4	6		3	3		5	4	
STOMACH	2	3		4	4		3	2		6	6		3	3		6	6	
SMALL INTESTINE	3	3		3	4		3	3		5	4		2	3		6	6	
PANCREAS	3	3		4	4		3	2		5	6		3	3		6	6	
LARGE INTESTINE	1	3		3	1		3	3		6	6		2	3		6	6	
Nematodiasis										1								
Enteritis, Acute																		
LIVER	3	3		4	4		3	3		5	6		3	3		6	6	
Hepatitis, Focal	1			1	1					1	1							
Infarct, Lobar																		
ADRENAL	3	3		3	4		2	2		6	6		3	3		6	6	

STRAIN OF RAT: Colony
 EXPOSURE: 13 wks
 AGENT: White Phosphorus/Feit

TABLE 3 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
 SMOKE II

	HIGH DOSE						MEDIUM DOSE						LOW DOSE					
	CONTROL			EXPOSED			CONTROL			EXPOSED			CONTROL			EXPOSED		
	M	F		M	F		M	F		M	F		M	F		M	F	
NUMBER OF ANIMALS	3	3		4	4		3	3		6	6		3	3		6	6	
THYROID	3	3		3	2		3	2		5	6		3	2		4	4	
Degeneration	3	3		1			3	2		5	6		2	1		4	4	
THYMUS	2	3		4	3		3	3		5	5		3	3		6	6	
Hemorrhage, Focal																		
KIDNEY	3	3		4	4		3	3		6	6		3	3		6	6	
Hydronephrosis																		
Nephritis, Interstitial	1						1						1					
Glomerulonephritis																		
Tubular Mineralization, Focal	1			3			1			2			3			3		
Tubular Dilatation, Focal										1								
Proteinuria	1									2						1	1	
BLADDER	1	1		4	4		0	1		5	2		3	1		5	4	
Perivascularitis																		
OVARY	0	2		0	3		0	3		0	5		0	3		0	6	
UTERUS	0	2		0	4		0	2		0	4		0	3		0	5	
Metritis																		

TABLE 4 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II

STRAIN OF RAT: Colony
EXPOSURE: 13 wks
AGENT: White Phosphorus/Talc

Appendix E

	HIGH DOSE				MEDIUM DOSE				LOW DOSE			
	CONTROL		EXPOSED		CONTROL		EXPOSED		CONTROL		EXPOSED	
	M	F	M	F	M	F	M	F	M	F	M	F
NUMBER OF ANIMALS	3		4	4	3	3	5	6	3	3	6	6
MAMMARY GLAND	0	0	0	0	2		0	3	0	3	0	3
Adenoma												
Mastitis												
TESTES	3	0	4	0	3	0	6	0	3	0	6	0
PROSTATE	0	0	4	0	3	0	6	0	3	0	6	0
Prostatitis									2			
MARROW	3	2	4	3	3	3	5	6	3	3	6	6
Granulopoiesis, Accelerated												
SPLEEN	2	2	4	4	3	3	6	5	2	3	6	5
Hemosiderosis	2		3	3			3	4	3		4	
BRAIN	3	3	4	4	3	2	6	6	3	3	6	6
Encephalitis, Pyogranulomatous												
Necrosis, Focal	3	3	4	4	3	3	6	5	3	3	6	6
EYE	2	2	3	3	3	2	5	6	3	3	6	6
PITUITARY												
Adenoma												

TABLE 5 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II

STRAIN OF RAT: Colony
EXPOSURE: 12 wks
DOSE LEVEL: Control
AGENT: White Phosphorus/Felt

	MALE						FEMALE					
	HIGH			MED			HIGH			MED		
	78-833	A	B	C	78-870	A	B	C	78-834	A	B	C
NASAL TURBINATE	-	-	-	-	-	-	-	-	-	-	-	-
Rhinitis, Focal												
LARYNX	-	-	-	-	-	-	-	-	-	-	-	-
Laryngitis												
Submucosal Gland Duct Ectasia	2								2			
TRACHEA	+	-	+	-	-	-	-	-	+	-	-	-
Tracheitis												
Submucosal Gland Duct Ectasia												
LUNGS	-	-	-	-	-	-	-	-	-	-	-	-
Pneumonia, Interstitial												
Pneumonia, Granulomatous												
Pneumonia, Purulent												
Congestion												
Peribronchiolar Lymphoid	1	1	1	2	1	1	1	1	1	1	1	2
Aggregates												
Bronchitis												

TABLE 6 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE 11

STRAIN OF RAT: Colony
EXPOSURE: 13 wks.
DOSE LEVEL: Control
AGENT: White Phosphorus/fe't

	MALE									FEMALE								
	HIGH			MED			LOW			HIGH			MED			LOW		
	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
HEART	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Myocardial Fibrosis, Focal																		
Myocarditis, Focal																		
ESOPHAGUS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
STOMACH	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
SMALL INTESTINE	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-
PANCREAS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
LARGE INTESTINE	+	-	+	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-
Nematodiasis																		
Enteritis, Acute																		
LIVER	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hepatitis, Focal	1																	
Infarct, Lobar																		
ADRENAL	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-

TABLE 7 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SHOKE II

STRAIN OF RAT: Colony
EXPOSURE: 13 wks
DOSE LEVEL: Control
AGENT: White Phosphorus/Fe³⁺

	MALE						FEMALE					
	HIGH			LOW			HIGH			MED		
	78-833	78-870	78-959	78-834	78-872	78-960	78-833	78-870	78-959	78-834	78-872	78-960
	A B C	A B C	A B C	A B C	A B C	A B C	A B C	A B C	A B C	A B C	A B C	A B C
THYROID	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -
Degeneration	3 3 2	1 1 1	3 4	3 3 2	4 2	3						
THYMUS	+	- - -	- - -	- - -	- - -	- - -						
Hemorrhage, Focal												
KIDNEY	- - -	- - -	- - -	- - -	- - -	- - -						
Hydronephrosis												
Nephritis, Interstitial												
Glomerulonephritis												
Tubular Mineralization, Focal												
Tubular Dilatation, Focal												
Proteinuria												
BLADDER	+	- +	+	+	+	- -	- +	+	+	+	+	+
Perivasculitis												
OVARY	+	+	+	+	+	+	- +	-	-	-	-	-
UTERUS	+	+	+	+	+	+	- +	-	-	-	-	-
METRITIS												

TABLE 8 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II

STRAIN OF RAT: Colony
EXPOSURE: 13 wks
DOSE LEVEL: Control
AGENT: White Phosphorus/Felt

	MALE									FEMALE								
	HIGH			MED			LOW			HIGH			MED			LOW		
	78-833	78-833	78-833	78-870	78-870	78-870	78-959	78-959	78-959	78-834	78-834	78-834	78-872	78-872	78-872	78-960	78-960	78-960
MAMMARY GLAND	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
Adenoma	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	-	-	-
Mastitis																		
TESTES	-	-	-	-	-	-	-	-	-	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	+	-	-	-	-	-	-	+	+	+	+	+	+	+	+	+
Prostatitis																		
MARROW	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Granulopoiesis, Accelerated																		
SPLEEN	-	+	-	-	-	-	+	+	-	+	-	-	-	-	-	2	2	1
Hemosiderosis																		
BRAIN	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Encephalitis, Pyogranulomatous																		
Necrosis, Focal	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
EYE	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PITUITARY																		
Adenoma																		

TABLE 9 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II

STRAIN OF RAT: Colony
EXPOSURE: 13 wks
DOSE LEVEL: High (1000 mg/m³)
AGENT: White Phosphorus/Felt

FEMALE

MALE

		78-831				78-874				78-832				78-875			
		A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D
NASAL TURBINATE	3/3	+	-	-	-					-	-	+	-	-	-		
Rhinitis, Focal																	
LARYNX	2/2	-	+	+	-					-	+	-	+	+	+		
Laryngitis	3	3			3								3				
Submucosal Gland Duct Ectasia																	
TRACHEA	0/3	+	+	+	+					-	-	+	-	-	-		
Tracheitis									2		2		3	2	2		
Submucosal Gland Duct Ectasia																	
LUNGS	4/4	-	-	-	-					-	-	-	-	-	-		
Pneumonia, Interstitial					1						2						
Pneumonia, Granulomatous		1							2			2	1				2
Pneumonia, Purulent																	
Congestion																	
Peribronchiolar Lymphoid		2	2	1	1												1
Aggregates																	
Bronchitis												3					

*Animals exposed with this group but held for 8 days for physiology studies prior to necropsy; not included in figures at left or in study.

TABLE 10 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II

STRAIN OF RAT: Colony
EXPOSURE: 13 wks
DOSE LEVEL: High (1000 mg/m³)
AGENT: White Phosphorus/Felt

		MALE								FEMALE									
		78-831				78-874				78-832				78-875					
		A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D		
*Animals exposed with this group but held for 8 days for physiology studies prior to necropsy; not included in figures at left or in study.																			
HEART	4/4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Myocardial Fibrosis, Focal																			
Myocarditis, Focal					2														
ESOPHAGUS	3/3	-	-	+	-	-	-	-	+	-	-	-	-	+	-	-	-	-	-
STOMACH	4/4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
SMALL INTESTINE	3/4	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PANCREAS	4/4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
LARGE INTESTINE	3/1	-	+	-	-	-	-	-	-	-	-	-	+	-	+	+	-	-	-
Nematodiasis																			
Enteritis, Acute																			
LIVER		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hepatitis, Focal																1			
Infarct, Lobar																			
ADRENAL	3/4	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	+

TABLE 11 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II

STRAIN OF RAT: Colony
EXPOSURE: 13 wks
DOSE LEVEL: High (1000 mg/m³)
AGENT: White Phosphorus/Felt

	MALE								FEMALE							
	78-831				78-874				78-832				78-875			
	A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D
*Animals exposed with this group but held for 8 days for physiology studies prior to necropsy; not included in figures at left or in study.																
THYROID	3/2	-	-	+		-				+	-	+		-		
Degeneration																
THYMUS	4/3	-	-	-		-				+	-	-		-		
Hemorrhage, Focal														3		
KIDNEY	4/4	-	-	-		-				-	-	-		-		
Hydronephrosis																
Nephritis, Interstitial																
Glomerulonephritis																
Tubular Mineralization, Focal										1	1	1		1	1	1
Tubular Dilation, Focal																
Proteinuria																
BLADDER	4/4	-	-	-		-				-	-	-		-		
Perivasculitis																
OVARY	0/3													+	+	
UTERUS	0/4															
Metritis																

TABLE 12 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SIOKE II

STRAIN OF RAT: Colony
EXPOSURE: 13 wks
DOSE LEVEL: High (1000 mg/m³)
AGENT: White Phosphorus/Felt

MALE FEMALE

*Animals exposed with this group but held for 8 days for physiology studies prior to necropsy; not included in figures at left or in study.

	79-831	78-874	78-832	78-875
	A B C D	A B	A B C D	A B
MAMMARY GLAND				
Adenoma				
Mastitis				
TESTES	4/0			
PROSTATE	4/0			
Prostatitis				
MARROW	4/3			
Granulopoiesis, Accelerated				
SPLEEN	4/4			
Hemosiderosis				
BRAIN	4/4			
Encephalitis, Pyogranulomatous				
Necrosis, Focal				
EYE	4/4			
PITUITARY	3/3			
Adenoma				

TABLE 13 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SINKE II

Appendix E

TABLE 14 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II

STRAIN OF RAT: Colony
EXPOSURE: 13 wks
DOSE LEVEL: Medium (500 mg/m³)
AGENT: White Phosphorus/Feit

FEMALE
78-871

MALE
78-869

		A	B	C	D	E	F		A	B	C	D	E	F
HEART	6/6	-	-	-	-	-	-		-	-	-	-	-	-
Myocardial Fibrosis, Focal														
Myocarditis, Focal	3	3					3							
ESOPHAGUS	4/6	-	+	-	-	+	-		-	-	-	-	-	-
STOMACH	6/6	-	-	-	-	-	-		-	-	-	-	-	-
SMALL INTESTINE	5/4	-	-	-	-	-	+		-	+	-	-	-	+
PANCREAS	5/6	-	-	-	-	-	+		-	-	-	-	-	-
LARGE INTESTINE	6/6	-	-	-	-	-	-		-	-	-	-	-	-
Nematodiasis							P							
Enteritis, Acute														
LIVER	5/6	+	-	-	-	-	-		-	-	-	-	-	-
Hepatitis, Focal														
Infarct, Lobar														
ADRENAL	5/6	-	-	-	-	-	-		-	-	-	-	-	-

TABLE 15 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II

STRAIN OF RAT: Colony
EXPOSURE: 13 wks
DOSE LEVEL: Medium (500 mg/m³)
AGENT: White Phosphorus/Felt

MALE

FEMALE

78-869

78-871

	6/6	A	B	C	D	E	F		A	B	C	D	E	F
THYROID	5/6	-	+	-	-	-	-		-	-	-	-	-	-
Regeneration		2		2	1	4	2		3	2	3	3	3	3
THYMUS	5/5	-	-	-	-	+	-		-	+	-	-	-	-
Hemorrhage, Focal														
KIDNEY	6/6	-	-	-	-	-	-		-	-	-	-	-	-
Hydronephrosis														
Nephritis, Interstitial														
Glomerulonephritis														
Tubular Mineralization, Focal														
Tubular Dilatation, Focal														
Proteinuria		1			1									2
BLADDER	5/2	-	-	+	-	-	-		+	-	-	+	+	+
Perivesculitis														
OVARY	0/5								+	-	-	-	-	-
UTERUS	0/5								-	-	-	+	-	-
Metritis														

TABLE 16 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II

STRAIN OF RAT: Colony
EXPOSURE: 13 wks
DOSE LEVEL: Medium (500 mg/m³)
AGENT: White Phosphorus/Felt

MALE

78-869

FEMALE

78-871

	6/6	A	B	C	D	E	F		A	B	C	D	E	F
MAMMARY GLAND	0/3													
Adenoma														
Mastitis														
TESTES	6/0	-	-	-	-	-	-		-	+	+	+	-	-
PROSTATE	6/0	-	-	-	-	-	-							
Prostatitis														
MARROW	5/6	-	+	-	-	-	-		-	-	-	-	-	-
Granulopoiesis, Accelerated														
SPLEEN	6/5	-	-	-	-	-	-		-	-	-	+	-	-
Hemosiderosis									2	1	1	1	1	1
BRAIN	6/6	-	-	-	-	-	-		-	-	-	-	-	-
Encephalitis, Pyogranulomatous														
Necrosis, Focal	6/5	-	-	-	-	-	-		-	-	-	-	-	+
EYE	6/6	-	-	-	-	-	-		-	-	-	-	-	-
PITUITARY														
Adenoma														

TABLE 17: MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II

STRAIN OF RAT: Colony
EXPOSURE: 13 wks
DOSE LEVEL: Low (200 mg/m³)
AGENT: White Phosphorus/Fe₂O₃

FEMALE

78-958

MALE

78-957

	78-957						78-958					
	A	B	C	D	E	F	A	B	C	D	E	F
NASAL TURBINATE	6/6	-	-	-	-	-	-	-	-	-	-	-
Rhinitis, Focal												
LARYNX	1/4	+	-	+	+	+	+	-	+	-	-	-
Laryngitis								2				
Submucosal Gland Duct Ectasia								2	1	2	2	
TRACHEA	5/4	-	+	-	-	-	-	-	-	+	-	+
Tracheitis												
Submucosal Gland Duct Ectasia						3						
LUNGS	6/6	-	-	-	-	-	-	-	-	-	-	-
Pneumonia, Interstitial								1	1		2	
Pneumonia, Granulomatous												
Pneumonia, Purulent												
Congestion												
Peribronchiolar Lymphoid		1	1	1	2			1	1	2	1	1
Aggregates												
Bronchitis												

STRAIN OF RAT: Co only
 EXPOSURE: 13 wks
 DOSE LEVEL: Low (200 mg/m³)
 AGENT: White Phosphorus/Fe³⁺t

TABLE 15 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RA-5
 SMOKE II

MALE FEMALE

78-957

78-958

	A	B	C	D	E	F		A	B	C	D	E	F
HEART	6/6	-	-	-	-	-		-	-	-	-	-	-
Myocardial Fibrosis, Focal													
Myocarditis, Focal					1								
ESOPHAGUS	5/4	-	-	+	-	-		-	-	-	+	-	+
STOMACH	6/6	-	-	-	-	-		-	-	-	-	-	-
SMALL INTESTINE	6/6	-	-	-	-	-		-	-	-	-	-	-
PANCREAS	6/6	-	-	-	-	-		-	-	-	-	-	-
LARGE INTESTINE	6/6	-	-	-	-	-		-	-	-	-	-	-
Nematodiasis													
Enteritis, Acute													
LIVER	6/6	-	-	-	-	-		-	-	-	-	-	-
Hepatitis, Focal													
Infarct, Lobar													
ADRENAL	6/6	-	-	-	-	-		-	-	-	-	-	-

TABLE 10 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE II

STRAIN OF RAT: Colony
EXPOSURE: 13 wks
DOSE LEVEL: Low (200 mg/m³)
AGENT: White Phosphorus/Felt

MALE
78-957

FEMALE
78-958

	A	B	C	D	E	F		A	B	C	D	E	F
THYROID	4/4	-	+	-	+	-		-	+	-	-	-	+
Degeneration			2	2	2	2		2	1	1	2		
THYROID	5/5	-	-	-	-	-		-	-	-	-	-	-
Hemorrhage, Focal													
KIDNEY	6/6	-	-	-	-	-		-	-	-	-	-	-
Hydronephrosis													
Nephritis, Interstitial													
Glomerulonephritis													
Tubular Mineralization, Focal													
Tubular Dilatation, Focal													
Proteinuria													
BLADDER	5/4	-	-	-	+	-		-	-	+	-	+	-
Perivascularitis													
OVARY	0/6												
UTERUS	0/5												
Metritis													

TABLE 20 : MICROSCOPIC OBSERVATIONS IN TISSUES FROM COLONY RATS
SMOKE 11

STRAIN OF RAT: Colony
EXPOSURE: 13 wks
DOSE LEVEL: Low (200 mg/m³)
AGENT: White Phosphorus/Felt

MALE

FEMALE

	78-957						78-958					
	A	B	C	D	E	F	A	B	C	D	E	F
MAMMARY GLAND												
Adenoma												
Mastitis												
TESTES												
PROSTATE												
Prostatitis												
MARROW												
Granulopoiesis, Accelerated												
SPLEEN												
Hemosiderosis												
BRAIN												
Encephalitis, Pyogranulomatous												
Necrosis, Focal												
EYE												
PITUITARY												
Adenoma												

APPENDIX F

PATHOLOGY REPORT - 13-WEEK EXPOSURE AND 4-WEEK RECOVERY PERIOD

PATHOLOGY REPORT
PROJECT SMOKE II, WHITE PHOSPHORUS/FELT
INHALATION STUDY PERFORMED FOR THIRTEEN WEEKS IN
EDGEWOOD COLONY RATS
PROTOCOL NO. PEM 78-7

1. INTRODUCTION.

Male and female Edgewood area colony rats approximately six weeks old were exposed to high (1000 mg/m^3), medium (500 mg/m^3) and low (200 mg/m^3) dose levels of the agent White Phosphorus/Felt in the form of smoke. The above doses were administered 15 minutes a day, 5 days a week for a period of thirteen weeks. Thirty days following final exposure, the rats were killed by intraperitoneal injection of sodium pentobarbital and necropsied. Since each dose group was exposed on different calendar dates, separate control groups were utilized with each exposure group. Controls were placed in the exposure chamber for the same length of time each day as the exposed animals. Controls were necropsied concurrently with the exposed groups. All animals were housed in Building E3266 in standard laboratory animal facilities during non-exposure periods. Following necropsy, tissues were fixed in ten percent buffered formalin. The preserved tissues were submitted to the American HistoLab, for imbedding in paraffin, processing, and staining with hematoxylin and eosin. The following tissues from the high dose group and controls were processed for microscopic examination: nasal turbinate, larynx/trachea, lungs, heart, esophagus, salivary gland, stomach, small intestine, pancreas, large intestine, liver, adrenal, thyroid, thymus, kidney, bladder, ovary/testis, uterus, mammary gland, skin, muscle, prostate, bone marrow, bone, spleen, nerve, eye, brain, and pituitary. Turbinates were removed at necropsy for processing. The trachea was sampled from the proximal portion and lungs were sectioned randomly. The respiratory tracts only (target organ) consisting of nasal turbinates, trachea, larynx, and lungs were examined in medium and low dose groups.

2. RESULTS.

Significant findings were limited to the respiratory tract. These data are presented in Tables 1-3. Microscopic diagnoses from all tissues of high dose and control rats are presented in Tables 4-7. Respiratory tract lesions are presented from all other animals in Tables 8-13. Lesions were noted in the larynx or trachea of 15 of 16 high (1000 mg/m^3) dose level rats, 20 of 24 medium dose (500 mg/m^3) level rats and in none of the controls. Pulmonary lesions were noted in 11 of 16 high dose rats, 6 of 24 medium dose rats and none of the controls for these two groups. Although none of the low dose animals exhibited significant lesions, one control (79-0176) for this group did display the same pulmonary lesion as the high and medium dose exposed animals. Lesions were most extensive and severe in the larynx and trachea. They consisted mainly of thickening of the lamina propria and submucosa by collagen, endothelial cell proliferation, and macrophage infiltration. Areas of collagen were tinctorially different and characterized by an amphophilic to basophilic appearance. Epithelioid macrophages with giant cell formation surrounded some of the altered collagen. Overlying epithelium often lacked cilia and was at times thickened and metaplastic. Occasionally, inflammatory cells were seen

in the epithelium. Similar but much less extensive lesions were seen in bronchi and bronchioles. These lesions were characterized by focal areas of altered collagen within the lamina propria. These foci were amphophilic to basophilic in appearance and occasionally surrounded by macrophages and epithelioid giant cells. Small granulomas were noted within respiratory bronchioles. These granulomas often extended into the adjacent lung parenchyma. The granulomas were characterized by swirling configurations of histiocytes and epithelioid macrophages with giant cell formation.


3. DISCUSSION.

A number of incidental lesions were observed in various organs of the high (1000 mg/m³) dose group. These lesions either occurred sporadically or with equal frequency in both exposed and control animals. Smoke-related lesions were limited to the upper airways and to a lesser extent, the smaller airways of the lung and the parenchyma adjacent to the terminal bronchioles. Since only the respiratory system was involved in the high dose animals, examination was confined to this system in the medium and low dose groups. All lesions attributable to the smoke were of a chronic inflammatory nature, characterized by collagen degeneration, and thickening of the lamina propria and submucosa of airways by fibrovascular proliferations.

Nasal lesions consisting of focal squamous metaplasia and a slight inflammatory cell infiltrate were seen in one high dose animal, accession number 78-910F. It is felt that lesions may have been present in other exposed animals as well; however, the sampling technique precluded our observing this. In light of this, it is recommended that a more systematic approach to studying the upper respiratory tract lesions be followed in subsequent studies.

4. CONCLUSION.

Rats exposed to the agent, White Phosphorus/Felt at the 1000 mg/m³ and 500 mg/m³ dosage levels developed a dosage related response characterized by chronic inflammation of the airways; lesions were most severe in the larynx and trachea but also involved the lower areas to a slight degree.


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30 May 1980

REVIEWED BY:



WILLIAM C. HALL, MAJ, VC
U.S. Army
USAMRIID

TABLE 1 MICROSCOPIC OBSERVATIONS FROM RESPIRATORY TISSUES FROM
EDGEWOOD AREA COLONY RATS EXPOSED TO WHITE PHOSPHORUS/FELT
SMOKE FOR 13 WEEKS AND KILLED 30 DAYS POST EXPOSURE

PROTOCOL NO. PEM 78-7		MALE		FEMALE	
SEX		1000PPM	CONTROL	1000PPM	CONTROL
DOSE					
ACCESSION NO.		78-910	78-912	78-913	78-914
NO. OF RATS		9	6	7	6
<u>DIAGNOSIS</u>					
Laryngitis/Tracheitis		9	0	6	0
Bronchitis/Bronchiolitis		4	0	2	0
Granulomatous Bronchiolitis/Pneumonia		3	0	2	0

TABLE 2 MICROSCOPIC OBSERVATIONS FROM RESPIRATORY TISSUES FROM
EDGEWOOD AREA COLONY RATS EXPOSED TO WHITE PHOSPHORUS/FELT
SMOKE FOR 13 WEEKS AND KILLED 30 DAYS POST EXPOSURE

PROTOCOL NO. PEM 78-7		SEX		MALE		FEMALE	
				500PPH	CONTROL	500PPH	CONTROL
ACCESSION NO.				78-926	78-927	78-929	78-930
NO. OF RATS				12	6	12	6
<u>DIAGNOSIS</u>							
Laryngitis/Tracheitis				10	0	10	0
Bronchitis/Bronchiolitis				4	0	1	0
Granulomatous Bronchiolitis/Pneumonia				0	0	1	0

TABLE 3 MICROSCOPIC OBSERVATIONS FROM RESPIRATORY TISSUES FROM
EDGEWOOD AREA COLONY RATS EXPOSED TO WHITE PHOSPHORUS/FELT
SMOKE FOR 13 WEEKS AND KILLED 30 DAYS POST EXPOSURE

PROTOCOL NO. PEM 78-7		MALE		FEMALE	
SEX					
DOSE		200PPM	CONTROL	200PPM	CONTROL
ACCESSION NO.		79-017	79-017	79-016	79-018
NO. OF RATS		6	3	6	2
<u>DIAGNOSIS</u>					
Laryngitis/Tracheitis		0	0	0	0
Bronchitis/Bronchiolitis		0	0	0	0
Granulomatous Bronchiolitis/Pneumonia		0	1	0	0

PROTOCOL NO.: PEM 78-7
 SEX: MALE
 EXPOSURE: CONTROL
 AGENT: WHITE PHOSPHORUS/FELT
 LENGTH OF EXPOSURE: 13 WEEKS
 POST EXPOSURE: 30 DAYS

TABLE 4 MICROSCOPIC OBSERVATIONS IN TISSUES FROM EDGEWOOD AREA COLONY RATS
 SMOKE II

Appendix F

ACCESSION NO.

DIAGNOSIS

78-912A

Histocytosis, focal, minimal, pleura, lung, rat
 Nephrosis, multifocal, minimal to mild, kidney
 Congestion, minimal, thymus

78-912B

Congestion, mild, lung, rat
 Hemorrhage and congestion, minimal, thymus

78-912C

Pyelitis, focal, acute, minimal, kidney, rat
 Hemorrhage and congestion, diffuse, mild, thymus

78-912D

Congestion, multifocal, mild, lung, rat
 Chronic respiratory disease, minimal, lung & bronchus
 Congestion and hemorrhage, diffuse, minimal, thymus

78-912E

Congestion, multifocal, mild, lung, rat
 Chronic respiratory disease, minimal, lung
 Hemorrhage, multifocal, minimal, thymus

78-912F

Lymphoid infiltrate focal, minimal, subplural, lung, rat
 Chronic respiratory disease, minimal, lung
 Congestion, diffuse, minimal, thymus
 Hemorrhage, multifocal, minimal, thymus
 Medial calcification, focal, minimal, pulmonary artery

TABLE 5 MICROSCOPIC OBSERVATIONS IN TISSUES FROM EDGEWOOD AREA COLONY RATS
SMOKE II

PROTOCOL NO.: PEM 78-7
SEX: FEMALE
EXPOSURE: CONTROL
AGENT: WHITE PHOSPHORUS/FELT
LENGTH OF EXPOSURE: 13 WEEKS
POST EXPOSURE: 30 DAYS

<u>ACCESSION NO.</u>	<u>DIAGNOSIS</u>
78-914A	Histiocytosis, focal, minimal, lung, rat Nephrocalcinosis, minimal, kidney Hemorrhage, multifocal, minimal, thymus
78-914B	Congestion, multifocal, mild, lung, rat Nephrocalcinosis, minimal, kidney Hemorrhage, multifocal, minimal, thymus
78-914C	Nephrocalcinosis, minimal, kidney, rat
78-914D	Congestion, multifocal, mild, lung, rat Retinal atrophy, focal, minimal, eye Endocardiosis, valvular, minimal, heart
78-914E	Tracheitis, focal, lymphocytic, minimal, trachea, rat Chronic respiratory disease, minimal, lung Congestion, focal, minimal, lung Granuloma, focal, Hardarian gland Congestion, diffuse, moderate, thymus

TABLE 5 MICROSCOPIC OBSERVATIONS IN TISSUES FROM EDGEWOOD AREA COLONY RATS
SMOKE II

PROTOCOL NO.: PEM 78-7
SEX: FEMALE
EXPOSURE: CONTROL
AGENT: WHITE PHOSPHORUS/FELT
LENGTH OF EXPOSURE: 13 WEEKS
POST EXPOSURE: 30 DAYS

DIAGNOSIS

Congestion, focal, minimal, lung, rat
Congestion and hemorrhage, diffuse, mild, thymus
Congestion, moderate, lymph node

ACCESSION NO.

78-974F

TABLE 6 MICROSCOPIC OBSERVATIONS IN TISSUES FROM EDGEWOOD AREA COLONY RATS
SMOKE II

PROTOCOL NO.: PEM 78-7
SEX: MALE
EXPOSURE: 1000 MG/M³
AGENT: WHITE PHOSPHORUS/FELT
LENGTH OF EXPOSURE: 13 WEEKS
POST EXPOSURE: 30 DAYS

ACCESSION NO.

DIAGNOSIS

Tracheitis, chronic, diffuse, moderate, trachea, rat
Interstitial pneumonia, multifocal, mild, lung
Congestion, diffuse, minimal, spleen

Tracheitis, chronic, diffuse, mild, trachea, rat
Prostatitis, interstitial, subacute, diffuse, minimal-mild, prostate
Epicarditis, subacute, focal, mild, rt. ventricle, heart

Tracheitis, chronic, diffuse, mild, trachea, rat
Prostatitis, interstitial, subacute, diffuse, minimal, prostate
Nematodiasis, large intestine, compatible with Oxyuriasis

Tracheitis, subacute, diffuse, moderate-severe, trachea, rat
Pneumonia, granulomatous, multifocal, minimal, lung
Prostatitis, subacute, multifocal, minimal, prostate
Congestion, diffuse, minimal, thymus

78-910A

78-910B

78-910C

78-910D

PROTOCOL NO.: PEM 78-7
 SEX: MALE
 EXPOSURE: 1000 MG/M³
 AGENT: WHITE PHOSPHORUS/FELT
 LENGTH OF EXPOSURE: 13 WEEKS
 POST EXPOSURE: 30 DAYS

TABLE 6 MICROSCOPIC OBSERVATIONS IN TISSUES FROM EDGEWOOD AREA COLONY RATS
 SMOKE II

Appendix F

ACCESSION NO.

DIAGNOSIS

78-910E

Tracheitis, chronic, multifocal, mild, trachea, rat
 Laryngitis, chronic, multifocal, mild, larynx
 Bronchitis, chronic, multifocal, mild, lung
 Rhinitis, focal, subacute, mild, nasal cavity
 Myocarditis, focal, subacute, minimal, heart
 Congestion, diffuse, mild, spleen

78-910F

Tracheitis, multifocal, chronic, mild, trachea, rat
 Pneumonia, granulomatous, multifocal, minimal, lung
 Bronchitis, multifocal, chronic, minimal, lung
 Prostatitis, interstitial, multifocal, minimal, prostate
 Congestion, and hemorrhage, diffuse, mild, thymus

78-910G

Tracheitis, multifocal, chronic, minimal, trachea, rat
 Bronchiolitis, chronic, multifocal, minimal, lung
 Prostatitis, subacute, multifocal, mild, prostate

78-910H

Laryngitis, chronic, diffuse, minimal, larynx, rat
 Pneumonia, granulomatous, multifocal, minimal, lung
 Hemorrhage, focal, minimal, thymus, rat

PROTOCOL NO.: PEM 78-7
SEX: MALE
EXPOSURE: 1000 MG/M³
AGENT: WHITE PHOSPHORUS/FELT
LENGTH OF EXPOSURE: 13 WEEKS
POST EXPOSURE: 30 DAYS

TABLE 6 MICROSCOPIC OBSERVATIONS IN TISSUES FROM EDGEWOOD AREA COLONY RATS
SMOKE II

ACCESSION NO.

78-9101

DIAGNOSIS

Laryngitis, diffuse, chronic, mild, larynx, rat
Pneumonia, granulomatous, multifocal, minimal, lung
Bronchiolitis, obliterative, focal, lung
Bronchiolitis, multifocal, chronic, minimal
Congestion, diffuse, mild, thymus
Congestion, diffuse, minimal, spleen

TABLE 7 MICROSCOPIC OBSERVATIONS IN TISSUES FROM EDGEWOOD AREA COLONY RATS
SMOKE II

PROTOCOL NO.: PEM 78-7
SEX: FEMALE
EXPOSURE: 1000 MG/M³
AGENT: WHITE PHOSPHORUS/FELT
LENGTH OF EXPOSURE: 13 WEEKS
POST EXPOSURE: 30 DAYS

Appendix F

ACCESSION NO.

DIAGNOSIS

78-913A

Tracheitis, chronic, multifocal, mild, trachea, rat
Hemorrhage, multifocal, minimal, thymus
Congestion, multifocal, mild, lung
Nephrocalcinosis and lithiasis, mild, kidney

78-913B

Laryngitis, multifocal, chronic, mild, larynx, rat
Bronchitis, multifocal, chronic, minimal, lung
Pneumonia, granulomatous, focal, minimal, lung
Nephrocalcinosis, minimal, kidney
Atrophy, focal, minimal, retina, eye
Congestion, and hemorrhage, diffuse, minimal, thymus

78-913C

Bronchitis, focal, chronic, minimal, lung, rat
Congestion, and hemorrhage, diffuse, mild, thymus
Myocarditis, focal, subacute, minimal, Rt. ventricle, heart
Nephrocalcinosis, minimal, kidney

PROTOCOL NO.: PEM 78-7
 SEX: FEMALE
 EXPOSURE: 1000 MG/M³
 AGENT: WHITE PHOSPHORUS/FELT
 LENGTH OF EXPOSURE: 13 WEEKS
 POST EXPOSURE: 30 DAYS

TABLE 7 MICROSCOPIC OBSERVATIONS IN TISSUES FROM EDGEWOOD AREA COLONY RATS
 SMOKE II

Appendix F

ACCESSION NO.

DIAGNOSIS

78-913D

Laryngitis, subacute, multifocal, minimal, larynx, rat
 Histiocytosis, multifocal, minimal, lung
 Hemorrhage, diffuse, moderate, lymph node
 Congestion, and hemorrhage, diffuse, mild, thymus

78-913E

Tracheitis, chronic, focal, minimal, trachea, rat
 Lymphoid infiltrate: focal, minimal, subpleural, lung
 Histiocytosis, focal, minimal, lung, rat
 Congestion, and hemorrhage, diffuse, mild, thymus
 Nephrocalcinosis, minimal, kidney
 Mineralization, focal, minimal, adrenal

78-913F

Tracheitis, focal, chronic, minimal, trachea, rat
 Congestion, diffuse, mild, thymus
 Cyst, thymus
 Hemorrhage, diffuse, moderate, lymph node
 Nephrocalcinosis, mild, kidney

TABLE 7 MICROSCOPIC OBSERVATIONS IN TISSUES FROM EDGEWOOD AREA COLONY RATS
SMOKE II

PROTOCOL NO.: PEM 78-7
SEX: FEMALE
EXPOSURE: 1000 MG/M³
AGENT: WHITE PHOSPHORUS/FELT
LENGTH OF EXPOSURE: 13 WEEKS
POST EXPOSURE: 30 DAYS

DIAGNOSIS

Laryngitis, multifocal, chronic, minimal, larynx, rat
Pneumonia granulomatous, multifocal, minimal, lung
Chronic respiratory disease, minimal
Congestion, diffuse, mild, lung
Medial calcification, multifocal, minimal, pulmonary artery
Hemorrhage and congestion, thymus

ACCESSION NO.

78-9136

PROTOCOL NO.: PEM 78-7
 SEX: MALE
 EXPOSURE: CONTROL
 AGENT: WHITE PHOSPHORUS/FELT
 LENGTH OF EXPOSURE: 13 WEEKS
 POST EXPOSURE: 30 DAYS

TABLE 8 MICROSCOPIC OBSERVATIONS IN RESPIRATORY TISSUES FROM EDGEWOOD AREA COLONY RATS SMOKE II

<u>ACCESSION NO.</u>	<u>DIAGNOSIS</u>
78-927A	Congestion, mild, lung, rat
78-927B	Congestion, mild, lung, rat
78-927C	No significant lesion
78-927D	Medial calcification, focal, minimal, pulmonary artery, rat
78-927E	Congestion, mild, lung, rat Medial calcification, multifocal, minimal, pulmonary artery Chronic respiratory disease, mild, lung
78-927F	Lymphoid infiltrate, focal, minimal, pleura, lung, rat Congestion, minimal, lung

TABLE 9 MICROSCOPIC OBSERVATIONS IN RESPIRATORY TISSUES FROM EDGEWOOD AREA COLONY RATS
SMOKE II

PROTOCOL NO.: PEM 78-7
SEX: MALE
EXPOSURE: 500 MG/M³
AGENT: WHITE PHOSPHORUS/FELT
LENGTH OF EXPOSURE: 13 WEEKS
POST EXPOSURE: 30 DAYS

ACCESSION NO.

DIAGNOSIS

78-926A

Tracheitis, chronic, diffuse, mild, trachea, rat
Bronchiolitis, focal, chronic, minimal, lung
Medial calcification, focal, minimal, pulmonary artery, lung

No significant lesion

78-926B

Tracheitis, diffuse, chronic, moderate, trachea, rat
Bronchitis, focal, chronic, minimal, lung

78-926C

Tracheitis, diffuse, chronic, moderate, trachea, rat
Bronchitis, multifocal, chronic, minimal, bronchi
Chronic respiratory disease, minimal, lung
Medial calcification, multifocal, minimal, pulmonary artery, lung

78-926D

Tracheitis, focal, chronic, moderate, trachea, rat
Medial hypertrophy, multifocal, moderate, pulmonary artery, lung

78-926E

Laryngitis, diffuse, chronic, mild, larynx, rat

78-926F

PROTOCOL NO.: PEM 78-7 TABLE 9 MICROSCOPIC OBSERVATIONS IN RESPIRATORY TISSUES FROM EDGEWOOD AREA COLONY RATS
SEX: MALE
EXPOSURE: 500 MG/M³
AGENT: WHITE PHOSPHORUS/FELT
LENGTH OF EXPOSURE: 13 WEEKS
POST EXPOSURE: 30 DAYS

Appendix F

<u>ACCESSION NO.</u>	<u>DIAGNOSIS</u>
78-926G	Tracheitis, diffuse, chronic, moderate, trachea, rat
78-926H	Bronchiolitis, focal, chronic, minimal, lung, rat
78-926I	Tracheitis, multifocal, chronic, moderate, trachea, rat Histiocytosis, multifocal, minimal, lung
78-926J	Laryngitis, multifocal, chronic, minimal, larynx, rat Medial calcification, focal, minimal, pulmonary artery, lung
78-926K	Tracheitis, multifocal, chronic, moderate, trachea, rat
78-926L	Tracheitis, focal, chronic, mild, trachea, rat

PROTOCOL NO.: PEM 78-7 TABLE 10 MICROSCOPIC OBSERVATIONS IN RESPIRATORY TISSUES FROM EDGEWOOD AREA COLONY RATS
SEX: FEMALE
EXPOSURE: 500 MG/M³
AGENT: WHITE PHOSPHORUS/FELT
LENGTH OF EXPOSURE: 13 WEEKS
POST EXPOSURE: 30 DAYS

SMOKE II

ACCESSION NO.	DIAGNOSIS
78-929A	Tracheitis, multifocal, chronic, minimal, trachea, rat Bronchiolitis, granulomatous, focal, minimal, lung
78-929B	Interstitial pneumonia, focal, minimal, lung, rat
78-929C	Essentially normal tissues, rat
78-929D	Tracheitis, focal, chronic, minimal, trachea, rat
78-929E	Laryngitis, focal, chronic, minimal, larynx, rat
78-929F	Tracheitis, diffuse, chronic, moderate, trachea, rat
78-929G	Laryngitis, focal, chronic, minimal, larynx, rat
78-929H	Laryngitis, focal, chronic, minimal, trachea, rat
78-929I	Laryngitis, focal, chronic, mild, larynx, rat
78-929J	Tracheitis, multifocal, chronic, minimal, trachea, rat

PROTOCOL NO.: PEM 78-7 TABLE 10 MICROSCOPIC OBSERVATIONS IN RESPIRATORY TISSUES FROM EDGEWOOD AREA COLONY RATS
SEX: FEMALE SMOKE 11

EXPOSURE: 500 MG/M³
AGENT: WHITE PHOSPHORUS/FELT
LENGTH OF EXPOSURE: 13 WEEKS
POST EXPOSURE: 30 DAYS

Appendix F

DIAGNOSIS

Tracheitis, multifocal, chronic, minimal, trachea, rat
Laryngitis, diffuse, chronic, minimal, larynx, rat
Bronchiolitis, focal, chronic, minimal, lung

ACCESSION NO.

78-929K

78-929L

PROTOCOL NO.: PEM 78-7 TABLE 11 MICROSCOPIC OBSERVATIONS IN RESPIRATORY TISSUES FROM EDGEWOOD AREA COLONY RATS
SEX: FEMALE SMOKE II

EXPOSURE: CONTROL
AGENT: WHITE PHOSPHORUS/FELT
LENGTH OF EXPOSURE: 13 WEEKS
POST EXPOSURE: 30 DAYS

<u>ACCESSION NO.</u>	<u>DIAGNOSIS</u>
78-930A	Histiocytosis, focal, minimal, lung, rat Chronic respiratory disease, minimal, lung
78-930B	Chronic respiratory disease, minimal, lung, rat
78-930C	Histiocytosis, multifocal, mild, lung, rat Chronic respiratory disease, lung
78-930D	Histiocytosis, multifocal, minimal, lung, rat Chronic respiratory disease, minimal, lung
78-930E	Histiocytosis, multifocal, minimal, lung, rat Chronic respiratory disease, lung

PROTOCOL NO.: PEM 78-7 TABLE 12 MICROSCOPIC OBSERVATIONS IN RESPIRATORY TISSUES FROM EDGEWOOD AREA COLONY RATS
SEX: MALE
EXPOSURE: 200 MG/M³
AGENT: WHITE PHOSPHORUS/FELT
LENGTH OF EXPOSURE: 13 WEEKS
POST EXPOSURE: 30 DAYS
SMOKE II

Appendix F

<u>ACCESSION NO.</u>	<u>DIAGNOSIS</u>
79-15A	No significant lesions
79-15B	No significant lesions
79-15C	No significant lesions
79-15D	No significant lesions
79-15E	No significant lesions
79-15F	No significant lesions

TABLE 13 MICROSCOPIC OBSERVATIONS IN RESPIRATORY TISSUES FROM EDGEWOOD AREA COLONY RATS
SMOKE II

PROTOCOL NO.: PEM 78-7
SEX: MALE
EXPOSURE: CONTROL
AGENT: WHITE PHOSPHORUS/FELT
LENGTH OF EXPOSURE: 13 WEEKS
POST EXPOSURE: 30 DAYS

Appendix F

DIAGNOSIS

Histiocytosis, focal, minimal, lung, rat
Congestion, minimal, lung
Chronic respiratory disease, minimal, lung
Medial calcification, focal, minimal, pulmonary artery, lung

Chronic respiratory disease, minimal, lung, rat
Congestion, minimal, lung

Pneumonia, granulomatous, multifocal, minimal, lung, rat
Chronic respiratory disease, lung

ACCESSION NO.

79-17A

79-17B

79-17C

PROTOCOL NO.: PEM 78-7 TABLE 14 MICROSCOPIC OBSERVATIONS IN RESPIRATORY TISSUES FROM EDGEWOOD AREA COLONY RATS
SEX: FEMALE SMOKE II

EXPOSURE: 200 MG/M³
AGENT: WHITE PHOSPHORUS/FELT
LENGTH OF EXPOSURE: 13 WEEKS
POST EXPOSURE: 30 DAYS

ACCESSION NO.

DIAGNOSIS

79-16A

Histiocytosis, focal, minimal, lung, rat
Pneumonia, interstitial, focal, minimal, lung

79-16B

Congestion, minimal, lung, rat

79-16C

Histiocytosis, multifocal, minimal, lung, rat
Lymphoid infiltrate, focal, minimal, lung

79-16D

Congestion, mild, lung, rat

79-16E

Medial calcification, focal, minimal, pulmonary artery, lung, rat

79-16F

Histiocytosis, multifocal, minimal, lung, rat

PROTOCOL NO.: PEM 78-7 TABLE 15 MICROSCOPIC OBSERVATIONS 1.4 RESPIRATORY TISSUES FROM EDGEWOOD AREA COLONY RATS
SEX: FEMALE
EXPOSURE: CONTROL
AGENT: WHITE PHOSPHORUS/FELT
LENGTH OF EXPOSURE: 13 WEEKS
POST EXPOSURE: 30 DAYS

Appendix F

<u>ACCESSION NO.</u>	<u>DIAGNOSIS</u>
79-18A	Chronic respiratory disease, minimal, lung, rat
79-18B	Congestion, minimal, lung, rat

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